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**Advanced Magnetic Resonance Imaging and Thermometry Techniques for
Guiding Thermal Therapies**

A dissertation submitted in partial satisfaction of the
requirements for the degree Doctor of Philosophy

in

Bioengineering

by

Qing Dai

2026

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ABSTRACT OF THE DISSERTATION

Advanced Magnetic Resonance Imaging and Thermometry Techniques for Guiding Thermal Therapies

by

Qing Dai

Doctor of Philosophy in Bioengineering

University of California, Los Angeles, 2026

Professor Holden H. Wu, Chair

Image-guided thermal therapies, including radiofrequency ablation (RFA), microwave ablation (MWA), and high-intensity focused ultrasound (HIFU), offer a curative option for patients with early-stage liver cancer who are not candidates for surgical resection or transplantation. These therapies deposit thermal energy through an interstitial applicator or an external transducer under image guidance to induce coagulative necrosis within the tumor. Magnetic resonance imaging (MRI) is uniquely suited to guide these procedures, providing superior soft-tissue contrast for treatment planning and targeting, continuous device guidance without ionizing radiation, non-invasive temperature mapping by proton resonance frequency (PRF) shift thermometry, and immediate post-procedural assessment of the ablation zone. An MRI-based workflow of planning, monitoring, and evaluation has been established and has demonstrated early feasibility.

However, wider adoption is limited by critical challenges at each stage of this workflow. For planning, computational models have been explored to simulate and predict the ablation zone, but they lack sufficient experimental validation. For monitoring, PRF thermometry of abdominal organs during energy delivery is compromised by respiratory motion and electromagnetic interference (EMI) from energy-delivery systems, both of which corrupt image quality and temperature measurements. For evaluation and targeting in therapies demanding high precision, such as MRI-guided HIFU, image contrast and sensitivity remain suboptimal for small features such as small tumors and tumor margins, and a contrast-enhancement technique operating in the clinically relevant therapeutic temperature range is lacking. As a result, the success of MRI-guided thermal therapy remains largely empirical and operator-dependent, restricting reproducibility and confining these procedures to a small number of specialized centers.

This dissertation addresses these technical challenges by developing and evaluating computational modeling, MR thermometry, and contrast-enhancement techniques for guiding thermal therapies. First, a joint computational–experimental framework was developed to characterize MWA energy-delivery strategies, validating the computational model against experimental measurements and supporting protocol optimization. Second, a volumetric PRF MR thermometry framework was developed that combines stack-of-radial MRI, image-based motion tracking, and image-navigated multi-baseline correction, extending temperature monitoring to near-full-liver coverage at high spatiotemporal resolution during breathing. Third, a software-driven active EMI suppression technique was developed that removes microwave-generator interference in the k-space domain, restoring image quality and reliable in vivo thermometry without hardware modification or interrupted heating. Fourth, a contrast-

enhancement technique was developed using thermoresponsive polymer-modified nanoparticles that reversibly modulate MRI contrast under HIFU stimulation, improving lesion detection at body temperature. Together, these advances could help move planning, monitoring, and evaluation from empirical practice toward a more quantitative, precise, and repeatable workflow, potentially supporting safer and more predictable MRI-guided thermal therapies and their broader clinical translation.

The dissertation of Qing Dai is approved.

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2026

DEDICATION

To Mom and Dad

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LIST OF ABBREVIATIONS

ACS	autocalibration signal
AES	active electromagnetic interference suppression
AZ	ablation zone
BCLC	Barcelona Clinic Liver Cancer
CC	correlation coefficient
CD	contrast difference
CEM43	cumulative equivalent minutes at 43 °C
CNR	contrast-to-noise ratio
CRLM	colorectal liver metastases
CT	computed tomography
DCE	dynamic contrast-enhanced
DLS	dynamic light scattering
DSC	Dice similarity coefficient
EMI	electromagnetic interference
EOE	end-of-expiration
EOI	end-of-inspiration
EPI	echo-planar imaging
FEM	finite-element method
FOV	field of view
FTIR	Fourier-transform infrared spectroscopy
FUS	focused ultrasound
Gd-DTPA	gadolinium diethylenetriamine pentaacetic acid
GRAPPA	generalized autocalibrating partially parallel acquisition
GRASP	golden-angle radial sparse parallel
GRE	gradient-recalled echo
HCC	hepatocellular carcinoma
HD95	95th-percentile Hausdorff distance
HIFU	high-intensity focused ultrasound
ICP-OES	inductively coupled plasma optical emission spectroscopy

IGTT	image-guided thermal therapy
iNAV	image-based navigator
iNAV-MB	image-navigated multi-baseline
KWIC	k-space weighted image contrast
LCST	lower critical solution temperature
LITT	laser-induced thermal therapy
LoA	limits of agreement
MEM	modulation enhancement map
MR	magnetic resonance
MRI	magnetic resonance imaging
MRIgHIFU	MRI-guided high-intensity focused ultrasound
MRT	magnetic resonance thermometry
MSN	mesoporous silica nanoparticle
MWA	microwave ablation
ND	noise decorrelation
PCA	principal component analysis
PDI	polydispersity index
PNIPAm	poly(N-isopropylacrylamide)
POx	poly(2-oxazoline)
PRF	proton resonance frequency
RF	radiofrequency
RFA	radiofrequency ablation
RMSE	root mean square error
ROI	region of interest
SAR	specific absorption rate
SB	single baseline
SD	standard deviation
SNR	signal-to-noise ratio
T1w	T1-weighted
T2w	T2-weighted
TE	echo time
TEM	transmission electron microscopy

tFp	temporal footprint
TGA	thermogravimetric analysis
tMAE	temporal mean absolute error
TR	repetition time
tRes	temporal resolution
tSD	temporal standard deviation
US	ultrasound
UV-Vis	ultraviolet-visible spectroscopy
VIBE	volumetric interpolated breath-hold examination

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1. Omar Curiel, Jing-Yuan Huang, Po-Chih Chen, Ji Ma, **Qing Dai**, Wenqi Zhou, David Lu, Holden H. Wu, Tsu-Chin Tsao. A master-slave robot manipulator for needle-based teleoperation in MRI chamber. arXiv preprint. doi: 10.48550/arXiv.2608.06354
2. **Qing Dai**, Jason Chiang, Shu-Fu Shih, Wenqi Zhou, David S. Lu, Holden H. Wu. Active electromagnetic interference suppression for MRI and proton resonance frequency shift thermometry during MRI-guided microwave ablation. *Magnetic Resonance in Medicine*. 2026. doi:10.1002/mrm.70440.
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 7. Xiaodong Zhong, Marcel Dominik Nickel, Stephan A. R. Kannengiesser, Brian M. Dale, Fei Han, Chang Gao, Shu-Fu Shih, **Qing Dai**, Omar Curiel, Tsu-Chin Tsao, Holden H. Wu, Vibhas Deshpande. Accelerated free-breathing liver fat and R2* quantification using multi-echo stack-of-radial MRI with motion-resolved multidimensional regularized reconstruction: initial retrospective evaluation. *Magnetic Resonance in Medicine*. 2024;92(3):1149–1161. doi:10.1002/mrm.30117.

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1. **Qing Dai**, Jason Chiang, Wenqi Zhou, David S. Lu, Holden H. Wu. Characterizing the spatiotemporal thermal effects of pulsed microwave ablation with computational modeling and MR thermometry. International Society for Magnetic Resonance in Medicine Annual Meeting, 2026, Cape Town, South Africa. (Oral, Magna Cum Laude)
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3. **Qing Dai**, Jason Chiang, Glen Nyborg, Shu-Fu Shih, David S. Lu, Holden H. Wu. Real-time MR thermometry to monitor microwave ablation and predict the ablation zone: Validation in an oncopig cancer model using immediate post-ablation MRI and gross pathology. International Society for Magnetic Resonance in Medicine Annual Meeting, 2025, Honolulu, HI, USA. p2189.

PATENTS

1. Holden H. Wu, **Qing Dai**. Active electromagnetic interference suppression for magnetic resonance imaging-guided intervention. U.S. Provisional Patent Application, filed March 2026. (Patent pending)
2. Holden H. Wu, Wenqi Zhou, **Qing Dai**, David S. Lu. Keypoint detection network for device localization on intra-procedural MRI. U.S. Provisional Patent Application, filed March 2026. (Patent pending)

CHAPTER 1 INTRODUCTION

1.1 Significance of image-guided thermal therapies for liver cancer treatment

Liver cancer is one of the most lethal malignancies worldwide: it is the sixth most diagnosed cancer and the third leading cause of cancer-related death, and its incidence continues to rise in many Western countries, including the United States^{1,2} (**Figure 1-1**). The majority of cases are hepatocellular carcinoma (HCC), a primary cancer originating in the liver, which accounts for approximately 75–85% of primary liver tumors³. Beyond primary liver cancer, the liver is also among the most common sites of metastatic spread, with colorectal liver metastases (CRLM) representing the most prevalent secondary liver tumor⁴. Prognosis remains poor across both primary and secondary settings, where the overall five-year relative survival rate is only about 22%, ranging from roughly 37% for localized disease to under 4% for distant metastatic disease, second only to pancreatic cancer⁵. Early detection and effective local intervention are therefore paramount to improving outcomes for liver cancer patients.

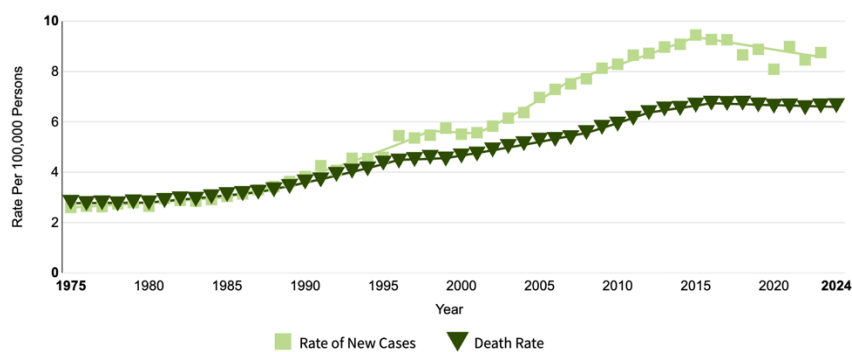


Figure 1-1. Liver cancer incidence has climbed since the 1990s while mortality has risen much more slowly, reflecting improved treatability of a historically lethal cancer. Age-adjusted incidence and death rates per 100,000 persons, 1975–2024. Data from SEER*Explorer, National Cancer Institute⁵.

When liver cancer is detected early, surgical resection has long been regarded as the curative gold standard. In practice, however, only an estimated 20–30% of patients are eligible for surgical resection, as the majority present with compromised liver function, multiple tumor sites, unfavorable tumor location, or comorbidities that preclude major surgery or general anesthesia^{6,7}. To address this gap, minimally invasive image-guided thermal therapies (IGTT), including microwave ablation (MWA) and radiofrequency ablation (RFA), have emerged over the past two decades as effective options for patients who are not surgical candidates. Performed percutaneously under image guidance, these procedures are typically completed within one to two hours under conscious sedation or local anesthesia, permit same-day discharge, and have demonstrated safety and efficacy comparable to resection for early-stage tumors^{6,8}. Their clinical role is formally established in the Barcelona Clinic Liver Cancer (BCLC) staging system, the most widely adopted framework for HCC management, which recommends thermal ablation as a first-line, curative-intent therapy for very-early-stage (BCLC 0) and early-stage (BCLC A) HCC in patients unsuitable for surgery⁶.

1.2 Physical principles and mechanisms of action of thermal therapy

Image-guided thermal therapies can be broadly divided into two regimes that differ in their mechanism of action and clinical objective: thermal ablation and hyperthermia. Thermal ablation uses very high temperatures to induce coagulative tissue necrosis outright, whereas hyperthermia applies sublethal heating for a longer period to achieve tumor cell death or as an adjuvant to other cancer treatments. Despite this difference, both regimes confront the same fundamental

challenge: depositing enough energy to treat the entire tumor target while sparing adjacent critical structures such as liver capsules, bile ducts, diaphragm, and bowel⁹.

1.2.1 Thermal ablation

Thermal ablation induces direct cell death by rapidly heating tissue to cytotoxic levels, typically above 50–60 °C, producing near-instantaneous coagulative necrosis through protein denaturation⁹. Its clinical objective is twofold: complete tumor eradication with an ablation margin of 5–10 mm in all directions, while sparing surrounding healthy tissue from collateral thermal injury^{10,11}. Clinically, ablative heating is delivered by radiofrequency (RFA), microwave (MWA), and laser ablation, all through a minimally invasive applicator inserted percutaneously into the tumor or by focused ultrasound (FUS), which is entirely non-invasive, concentrating acoustic energy from an external transducer onto a deep focal point, analogous to focusing sunlight with a magnifying glass.

These modalities differ in how energy is coupled into tissue. RFA passes an alternating electrical current (~450–500 kHz) through a needle electrode, agitating tissue ions to generate resistive (Joule) heating^{12,13}, whereas MWA emits electromagnetic waves (915 MHz or 2.45 GHz) from an interstitial antenna, driving water-molecule rotation to produce volumetric dielectric heating^{14,15}. Because RFA requires a closed electrical circuit through the tissue to generate resistive heating, whereas microwave energy radiates from the antenna and heats tissue water molecules directly, MWA shows several key advantages over RFA, including faster heating, higher temperatures, and larger coagulation volumes (especially with multi-antenna arrays), with reduced susceptibility to tissue charring and to heat-sink effects from adjacent vessels, leading to

its growing adoption over RFA for liver tumors^{13,15,16}. The resulting temperature distribution from MWA is governed by the coupled electromagnetic and bioheat-transfer processes that link energy deposition to tissue heating. FUS thermal ablation is also available for liver cancer treatment as well as in other organs such as breast¹⁷, bone¹⁸, and prostate¹⁹. A related non-thermal FUS-based ablation technique, histotripsy, which fragments tissue through acoustic cavitation rather than heat, was recently FDA-approved for liver tumors²⁰. **Table 1-1** compares ablation modalities in clinical practice.

1.2.2 Hyperthermia

In contrast, hyperthermia raises tissue temperature only moderately, to roughly 40–45 °C, sustained over a prolonged period of tens of minutes. At these sublethal temperatures, cells are not killed outright; instead, the heated microenvironment is sensitized, enhancing the efficacy of adjuvant chemotherapy and radiation through improved perfusion and oxygenation and impaired DNA repair²¹. In liver cancer, mild hyperthermia has been investigated primarily as a trigger for localized drug delivery, such as releasing doxorubicin from thermosensitive liposomes in combination with RFA or FUS^{1,22}.

Modality	Invasiveness	Energy Type	Energy Source	Frequency	Typical target temperature	MRI compatibility
Radiofrequency ablation (RFA)	Percutaneous	Hyperthermic; resistive Joule heating from ionic agitation	Alternating current via needle electrode	450–500 kHz	60–100 °C	MR-conditional; shaft artifact, broadband EMI, RF heating risk; imaging usually interleaved
Microwave ablation (MWA)	Percutaneous	Hyperthermic; dielectric heating from water-dipole rotation	Electromagnetic waves from interstitial antenna	915 MHz or 2.45 GHz	>100 °C	MR-conditional; antenna artifact; broadband EMI degrades real-time MRI and PRF thermometry (Chapter 4)
Laser induced thermal therapy (LITT)	Percutaneous	Hyperthermic; optical absorption converted to heat	Near-infrared light via optical fiber	980–1064 nm (near-infrared)	60–100 °C	MR-safe; non-metallic fiber, minimal artifact, no EMI
Cryoablation	Percutaneous	Hypothermic; freeze–thaw cycles cause ice-crystal injury and vascular thrombosis	Heat extraction by argon expansion or liquid nitrogen	NA; 2–3 freeze–thaw cycles	–20 to –40 °C lethal isotherm	MR-conditional; ice ball signal void delineates the treated volume; PRF thermometry difficult in the frozen regions
High intensity focused ultrasound (HIFU)	Noninvasive	Hyperthermic; acoustic absorption produces focal heat	Focused ultrasound from external transducer	~0.5–3 MHz (~1 MHz typical for abdominal)	>60 °C at the focus; 40–45 °C for mild hyperthermia (Chapter 5)	MR-compatible; no applicator artifact; established platform for MR thermometry–guided treatment
Histotripsy	Noninvasive	Non-thermal; cavitation bubble cloud liquefies tissue	High-amplitude ultrasound pulses from external transducer	~0.5–1 MHz with microsecond pulses at <1% duty cycle	NA	Ultrasound-guided; MR guidance preclinical; non-thermal, so PRF thermometry not applicable

Table 1-1. Comparison of clinical ablation modalities and their MRI compatibility.

1.3 Image-guidance and therapeutic modalities: technical overview

Despite this established role of IGTT, several studies report higher rates of local tumor progression and recurrence after ablation than after resection, largely due to insufficient ablation margins and incomplete tumor coverage²³. Efforts to close this gap have followed two tracks: (1) improving the therapeutic devices themselves, such as antenna and transducer design, and (2) improving the image guidance and computational tools that support them. This dissertation addresses the latter — advancing the planning, targeting, monitoring, and confirmation of thermal therapy so as to close the performance gap with surgery and extend thermal therapy to more challenging cases.

Because thermal therapies are minimally invasive or non-invasive, the interventional radiologist does not have direct visual access to the tumor and its surrounding anatomy, and must therefore rely on image guidance for both applicator placement (or HIFU focal point localization) and intraprocedural monitoring. Three medical imaging modalities are currently used clinically for thermal therapy guidance and monitoring: ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI).

Ultrasound is the most widely used image guidance modality for needle-based thermal therapies due to its real-time imaging capability, portability, and widespread availability in the procedure suite. However, ultrasound suffers from limited soft tissue contrast that may render tumor boundaries indistinct. For ablation monitoring, ultrasound relies on the hyperechoic appearance

of gas bubble formation from tissue vaporization²⁴, a surrogate marker that may not reliably predict the true ablation boundary. CT provides higher spatial resolution and broader anatomical coverage, with contrast-enhanced CT enabling tumor delineation and post-ablation evaluation. However, CT exposes patients to ionizing radiation, requires iodinated contrast agents with associated nephrotoxicity risk, and lacks the temporal resolution needed for real-time monitoring.

MRI offers unique advantages for thermal therapy guidance that set it apart from US and CT. First, MRI provides superior soft tissue contrast that enables direct visualization of tumor tissue against surrounding parenchyma without the need for contrast agents, allowing precise targeting even in challenging anatomies. Second, MRI offers flexible scan orientations and multi-parametric contrast mechanisms (T₁, T₂, diffusion, fat quantification) for comprehensive treatment planning and post-procedure assessment in situ. Third, and most importantly for monitoring, MRI is the only clinically adopted imaging modality that enables non-invasive, real-time, quantitative temperature mapping through proton resonance frequency (PRF) shift-based MR thermometry^{25,26}. This unique capability allows direct visualization of the ablation zone formation during treatment, supporting determination of treatment endpoint and protection of critical structures (**Figure 1-2**). MRI-guided HIFU is FDA-approved for treating uterine fibroids²⁷, bone metastases²⁸, essential tremor²⁹, breast¹⁷ and prostate cancer¹⁹. MRI-guided MWA and RFA, while their feasibility has been demonstrated³⁰, have yet to achieve broad clinical adoption.

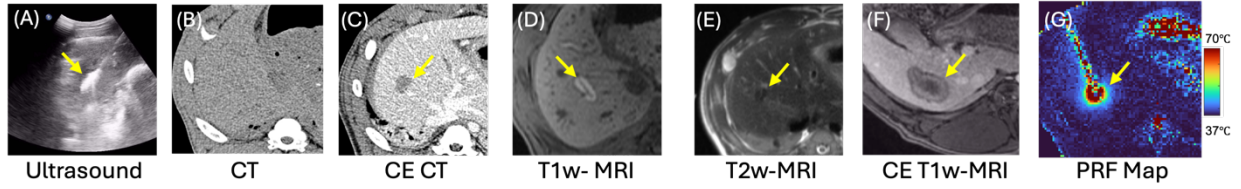


Figure 1-2. Multi-modal imaging of ablation zone (yellow arrow) from a healthy pig subject. MRI provides multi-parametric soft tissue contrast and non-invasive temperature mapping unavailable with US or CT. CE: contrast enhanced.

1.4 MRI technologies for guiding thermal therapies

MRI supports the full thermal therapy workflow (**Figure 1-3**): pre-procedural diagnosis and planning, intra-procedural device guidance, therapy delivery and monitoring, and post-procedural assessment. Each stage has different demands on spatial resolution, temporal resolution, and contrast, and distinct MRI acquisition and reconstruction strategies have been developed to meet them.



Figure 1-3. The MRI-guided thermal therapy workflow. Images show an exemplary case of MRI-guided microwave ablation from healthy pig subjects.

1.4.1 Treatment planning

Pre-procedural planning relies on diagnostic-quality 3D MRI to delineate the tumor, define an adequate ablation margin, and identify an applicator trajectory that avoids critical structures.

T1w gradient-echo acquisitions (e.g., VIBE³¹) are typically acquired under breath-hold and provide the anatomical and vascular detail needed to characterize the tumor extent and its relationship to major vessels and bile ducts. Non-Cartesian trajectories, particularly radial and stack-of-radial acquisitions such as Star-VIBE³², offer an alternative under free-breathing conditions owing to their inherent robustness to motion. T2w, diffusion-weighted, and dynamic contrast-enhanced (DCE) imaging further improve lesion conspicuity.

Beyond diagnostic imaging, computational modeling of the coupled electromagnetic and bioheat-transfer physics that govern energy deposition³³ is increasingly explored as a complementary planning tool, offering the potential to predict ablation-zone size and shape for a given applicator placement and energy-delivery protocol before treatment begins.

1.4.2 Device guidance and navigation

Once the target has been localized and a trajectory selected, intra-procedural MRI is performed to guide the applicator toward the target. Breath-hold 3D T1w-VIBE acquisitions provide volumetric coverage with high spatial fidelity, and the resulting volume can be reformatted along oblique multiplanar views aligned with the applicator trajectory, allowing the needle path and the target to be visualized in a single plane and the advancement confirmed in three dimensions³⁴.

Due to the limited space inside the MR scanner bore, which restricts the physician's in-bore access, a step-and-shoot workflow is often employed where volumetric imaging alternates with out-of-bore device advancement, rather than continuous tracking and insertion. Conversely, 2D GRE sequences can be acquired at near-real-time frame rates under respiratory gating or triggering along a fixed prescribed slice and exhibit pronounced susceptibility artifact near the

applicator. Balanced steady-state free precession (bSSFP)³⁰ offers higher SNR efficiency and stronger anatomical contrast for a comparable frame rate, but is prone to off-resonance banding artifacts, which worsen near metallic devices and at higher field strength.

1.4.3 Therapy monitoring: MR thermometry

Several MRI-based temperature measurement techniques have been investigated, including those based on T_1 relaxation time, T_2 relaxation time, the diffusion coefficient, and the proton resonance frequency (PRF) shift of water^{25,35}. Among these, PRF thermometry has become the clinical standard, due to its linearity over the temperature range relevant to thermal therapy, its near independence of tissue type in aqueous tissue, and its quantitative accuracy. Its principal limitation is that the PRF shift does not occur in adipose tissue.

The PRF method exploits the temperature dependence of the water proton chemical shift, which arises from temperature-induced changes in hydrogen bonding between water molecules. As temperature increases, hydrogen bonds stretch and break, increasing the electron screening of the water protons so that they experience a slightly reduced local magnetic field, and their resonance frequency decreases accordingly³⁵. As **Figure 1-4** shows, the temperature change is computed from the phase difference between a dynamic gradient-recalled echo (GRE) image and a baseline reference image as:

$$\Delta T = \frac{\phi(T) - \phi(T_0)}{\gamma \alpha B_0 T E} \quad (1-1)$$

where ϕ is MR phase image, T is the current time point during energy delivery, T_0 is a time point during non-heating baseline acquisition, $\alpha \approx -0.01$ ppm/°C is the PRF coefficient, γ is the gyromagnetic ratio, B_0 is the field strength, and TE is the echo time.

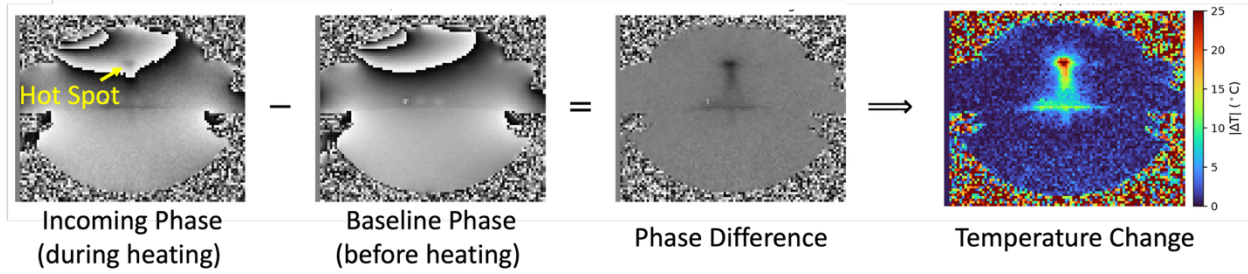


Figure 1-4. PRF MR thermometry principle. The phase difference between a baseline (pre-heating) and dynamic (during-ablation) gradient-recalled echo image is converted to a temperature-change map. An example is shown during MRI-guided HIFU where the yellow arrow indicates the ablated region.

GRE sequences are the workhorse for PRF thermometry because they preserve the phase information needed for temperature measurement and allow the echo time to be tuned to optimize temperature-to-noise ratio³⁶. Conventional 2D Cartesian GRE acquisitions provide robust thermometry in static or breath-held tissue but are limited in temporal resolution and volumetric coverage and are sensitive to motion-induced errors. Echo-planar imaging (EPI)³⁷ variants accelerate acquisition by sampling multiple k-space lines per excitation, achieving higher temporal resolution at the cost of geometric distortion. For volumetric coverage, 3D Cartesian GRE sequences add phase encoding along the slice direction, but the resulting acquisition times are often infeasible for dynamic imaging.

Non-Cartesian stack-of-radial sequences have emerged as an attractive alternative for dynamic MR thermometry, owing to their inherent robustness to motion and their flexibility in trading spatial resolution against temporal resolution. In golden-angle-ordered radial acquisitions³⁸, successive spokes are incremented by 111.25° , allowing dynamic image frames to be reconstructed retrospectively at arbitrary temporal resolution by re-grouping the acquired k-space data through sliding-window approaches with advanced reconstruction techniques such as k-space weighted image contrast (KWIC) filtering³⁹. The feasibility of 3D stack-of-radial thermometry has been established in tissues with limited motion, such as breast and prostate^{40,41}.

PRF thermometry is a phase-difference measurement and therefore requires a stable reference baseline. In static tissue, a single pre-heating reference image (single-baseline PRF) is sufficient. In moving tissue such as the abdomen, however, respiratory motion causes spatial misregistration between the dynamic and baseline images, introducing temperature errors that can exceed 10°C .³⁵ Multi-baseline approaches^{42,43}, which acquire a library of reference images across the respiratory cycle and dynamically select the best-matched baseline, have been developed to address this challenge.

While the instantaneous temperature map provides real-time feedback during ablation, the cumulative thermal effect on tissue is better predicted by the thermal dose, which integrates the temperature–time history. The most widely adopted model is the cumulative equivalent minutes at 43°C (CEM43)⁴⁴, for which a threshold of 240 minutes is commonly used to predict the boundary of irreversible coagulative necrosis. The Arrhenius model and simpler isotherm-based metrics for predicting thermal damage are also routinely used in research and clinical practice.

These thermal dose metrics derived from MR thermometry provide quantitative endpoints that bridge real-time intra-procedural measurements with the predicted treatment outcome.

1.4.4 MRI-guided theranostic imaging

Theranostic imaging refers to the integration of therapeutic action and diagnostic imaging within a single platform, typically through stimuli-responsive contrast agents or nanomaterials. In MRI-guided thermal therapy, the concept is most compelling where the HIFU treatment target is small, poorly visualized on conventional imaging contrast, or requires precise localization within sensitive anatomy. One promising approach is the use of thermoresponsive nanoparticles⁴⁵, which are fabricated to change physical state at a defined transition temperature. Such nanoparticles can be loaded with an MR contrast agent, a therapeutic agent, or both, so that localized HIFU-induced heating triggers a change in MRI contrast and, where a drug is carried, its release. Because only nanoparticles within the heated focal region are activated, the resulting enhancement is confined to the treatment site while nanoparticles in surrounding tissue remain unactivated. The target is thereby distinguished from adjacent tissue based on temperature rather than perfusion alone, providing direct confirmation that the HIFU focal point coincides with the intended target.

1.4.5 Post-treatment assessment and follow-up imaging

Post-treatment MRI confirms technical success and screens for early complications. The ablation zone typically appears hyperintense on non-contrast T1w images, reflecting coagulation necrosis, and hypointense on T2w images, reflecting tissue desiccation⁴⁶. Contrast-enhanced T1w MRI is

particularly well suited for margin assessment, where the tumor after ablation appears as a T1w hypointense “ghost” within a T1w hyperintense ablation zone¹³, directly visualizing the treatment margin and informing the decision for repeat treatment. Registration of pre- and post-procedural images further allows the minimal ablative margin to be measured directly, providing a quantitative check against the 5–10 mm target and identifying the under-treatment that underlies most local recurrences.

1.5 Current challenges in MRI-guided thermal therapies

Advances in thermal therapy devices and MRI guidance technologies have brought several MRI-guided thermal treatments into clinical practice, including for prostate⁴⁷ and breast cancer⁴⁸. Beyond these few approved applications, however, clinical adoption in abdominal interventions remains confined to a small number of large academic medical centers, constrained both by technical challenges, such as physiological motion, lengthy scan times, and limited sensitivity and specificity, and by accessibility barriers, such as specialized hardware and the unique skill set required. These challenges must be resolved before reliable temperature monitoring and safe, effective energy delivery can be achieved more broadly. The following sections examine four such challenges, spanning treatment planning, therapy monitoring, and target confirmation, that together motivate the specific aims of this dissertation.

1.5.1 MWA computational modeling lacks spatiotemporal temperature validation

Computational models for MWA simulate electromagnetic propagation and tissue bioheat transfer, and can be used to predict ablation zone size and shape to improve treatment

outcomes³³. For example, they have been used to optimize MWA energy delivery strategies to induce rounder ablation zones with less tissue charring⁴⁹. However, these models rely on simplified physical assumptions and tissue conditions, and require experimental validation. Previous studies have mainly focused on validation against gross tissue pathology, which provides only a single snapshot of tissue effects after the ablation concludes. The spatiotemporal thermal evolution of the ablation zone during treatment therefore remains under-characterized.

1.5.2 PRF thermometry in abdominal organs lacks volumetric coverage under respiratory motion

Respiratory motion in abdominal organs introduces a fundamental challenge for MR thermometry. Intra-frame tissue displacement causes spatial misregistration between the dynamic images and the baseline reference, producing phase errors that can appear as temperature changes exceeding 10 °C in non-heated regions³⁵. Multi-baseline PRF thermometry has been proposed to address this baseline mismatch by acquiring a library of reference images at different motion positions and matching each incoming dynamic image to the closest baseline^{42,50}. However, most multi-baseline methods are restricted to one to three 2D slices to balance spatiotemporal resolution, and such coverage cannot capture the full three-dimensional extent of ablation zone growth.

1.5.3 Electromagnetic interference from the MWA system degrades real-time MRI and MR thermometry

MRI-guided MWA faces a critical technical barrier from electromagnetic interference (EMI) generated by the MWA system. Commercial MWA generators emit broadband EMI during active ablation, which couples into the MRI receiver coils through imperfect shielding of the generator and cabling⁵¹. The resulting interference contaminates MRI k-space data and appears as noise-like artifacts in the reconstructed images, obscuring the ablation zone boundary and degrading PRF temperature measurements. Existing mitigation strategies rely either on hardware modifications^{52,53}, such as additional physical shielding or in-line RF filters which complicate clinical workflow and require customized assembly, or on intermittent protocols that pause energy delivery during image acquisition^{46,47}, disrupting the therapeutic dose and precluding true real-time monitoring during active ablation.

1.5.4 Conventional MRI contrast cannot confirm HIFU targeting in small or low-contrast lesions

MRI-guided HIFU delivers energy to a focal point on the order of 1.5 mm³, offering precise spatial control over both ablation and nanoparticle-mediated drug release¹⁸. Although MRI provides superior soft-tissue contrast compared with other imaging modalities, small tumors, tumor margins, and lesions with low intrinsic contrast remain difficult to delineate during energy delivery. Conventional gadolinium-based chelates provide static enhancement that reflects tissue vascularity, but do not respond to the therapeutic intervention and therefore cannot confirm that the HIFU focal point coincides with the intended target. Prior studies developed the Spotlight MRI technique⁵⁴, which pairs modulated HIFU sonication with thermoresponsive nanoparticles

that modulate T1 in response to focal heating, substantially amplifying the SNR and CNR of the targeted region. That platform, however, operates at a transition temperature of 32 °C, below physiological body temperature, and the feasibility of contrast modulation at physiological temperature has not been characterized.

1.6 Specific Aims and dissertation overview

The objective of this dissertation is to develop and evaluate advanced MRI and MR thermometry techniques to improve the planning, guidance, and monitoring of thermal therapies for cancer treatment. The work is organized around four specific aims, each addressing one of the technical challenges identified in Section 1.5.

Aim 1 (Chapter 2) develops and evaluates a joint computational–experimental framework for characterizing MWA energy-delivery strategies. A finite-element model coupling the electromagnetic wave and bioheat equations simulates microwave heating in tissue, and three energy-delivery protocols are performed on ex vivo porcine liver with simultaneous real-time MR thermometry at 3 T. Model predictions are validated against MRT-measured temperature fields and, using CEM43-derived ablation zones, against gross pathology, establishing a modeling–MRT–pathology workflow for model calibration and protocol optimization.

Aim 2 (Chapter 3) develops and evaluates a volumetric MR thermometry framework for moving tissues, combining a golden-angle-ordered 3D stack-of-radial MRI sequence with an image-navigated multi-baseline (iNAV-MB) PRF method. Two radial reconstruction techniques

— k-space weighted image contrast (KWIC) filtering and golden-angle radial sparse parallel (GRASP) MRI — are implemented and compared. The framework is validated through ex vivo motion phantom HIFU ablation experiments and in vivo non-heating swine experiments.

Aim 3 (Chapter 4) develops a software-based active EMI suppression (AES) framework for reliable MRI and MR thermometry during MRI-guided microwave ablation. The framework leverages auxiliary coil arrays with principal-component-based EMI source extraction and frame-by-frame adaptive suppression, and is compatible with standard multi-channel MRI reconstruction pipelines. The approach is evaluated through gel phantom and in vivo porcine MWA experiments at 3 T.

Aim 4 (Chapter 5) develops and evaluates a temperature-modulated MRI contrast enhancement platform for treatment target detection during MRI-guided HIFU-mediated nano-theranostics. Thermoresponsive polymer-modified mesoporous silica nanoparticles incorporating Gd-DTPA are designed with a lower critical solution temperature (LCST) tuned to physiological body temperature, enabling HIFU-stimulated contrast modulation at the focal point. The platform is evaluated through phantom and ex vivo tissue experiments using 3D stack-of-radial MRI with KWIC reconstruction and PRF thermometry.

Chapter 6 summarizes the contributions of this dissertation, discusses their limitations, and outlines directions for future work toward clinical translation.

CHAPTER 2 CHARACTERIZING MICROWAVE ABLATION ENERGY DELIVERY STRATEGIES USING COMPUTATIONAL MODELING AND MR THERMOMETRY

2.1 Introduction

Hepatocellular carcinoma (HCC) is among the most common causes of cancer-related mortality worldwide¹. For patients with very-early- and early-stage HCC, thermal ablation—including both radiofrequency ablation (RFA) and microwave ablation (MWA)—is a preferred, potentially curative treatment option⁶ that destroys cancer cells in situ by raising local temperatures beyond the threshold for irreversible cellular injury, offering a minimally invasive alternative to surgery with lower morbidity and the option for repeat treatment. Compared with the more established resistance-heating-based RFA, MWA uses a dielectric heating mechanism and is increasingly favored in clinical practice owing to several advantages: greater resilience to heat-sink effects from faster heating and higher peak temperatures well above 100 °C (up to ~150 °C), larger ablation zones achievable with multiple antennas, and—because no direct electrical circuit is formed in the tissue—heating that is less affected by tissue charring and changing impedance and is safe near metal implants.¹⁵ These advantages have made MWA increasingly popular for treating HCC⁵⁵ as well as many other solid tumors of the lung⁵⁶, kidney⁵⁷, bone⁵⁸, and thyroid⁵⁹.

The clinical objective of microwave ablation is to eradicate the tumor with a 5–10 mm ablation margin while sparing adjacent critical structures¹¹. To achieve adequate coverage, standard-of-care MWA protocols typically rely on a “brute-force” strategy of increasing the delivered power or extending the ablation time. However, the fast, high-temperature heating profile that makes MWA effective also makes it more prone to collateral thermal injury of adjacent critical

structures such as the liver capsule, diaphragm, bowel, or biliary tract²³. High power also tends to produce rapid heating preferentially along the longitudinal axis of the antenna, yielding an elongated, tear-drop-shaped necrotic zone with disproportionately limited radial (short-axis) growth⁶⁰. This can lead to insufficient short-axis coverage and incomplete margins around the tumor. Furthermore, high-power MWA is more likely to cause tissue charring and carbonization, which contribute to complications and procedural pain⁶¹. An energy-delivery strategy that balances the competing risks of over-treatment (collateral damage) and under-treatment (positive margins and recurrence) is therefore highly desirable for safe and effective liver tumor management.

Alternative energy-delivery strategies, such as pulsed MWA, have been proposed to address these shortcomings. By alternating active heating with passive cooling intervals, pulsed delivery allows transient tissue cooling between pulses⁶¹. Laboratory studies have reported that pulsed energy delivery promotes more uniform thermal diffusion away from the antenna and yields rounder, more symmetric ablation zones on gross pathology in ex vivo and in vivo liver models⁶², along with reduced near-field charring at high power⁴⁹. A range of pulsing schemes has been investigated, including varying duty cycle, “bookend” high-power phases, and ramped power profiles⁶³⁻⁶⁵. Clinical studies have additionally reported less procedural pain and lower complication rates with pulsed than with continuous heating^{61,66}.

Although these studies establish the promise of pulsed delivery, the way it has been evaluated leaves three important gaps. First, most studies assess only a small number of hand-picked protocol settings, providing limited insight into how the large space of pulsing parameters shapes

the outcome. Second, most studies compare only final gross-pathology dimensions, which capture a single end-state, or probe and thermocouple measurements, which capture a single location, rather than the transient spatiotemporal temperature and thermal-dose accumulation that drive lesion formation. As a result, it remains difficult to resolve the full temperature field, the progression of the ablation boundary, and how intermittent delivery influences heat accumulation and lesion growth. Third, wide heterogeneity among commercial MWA systems in antenna design, transmission losses, and active-cooling schemes contributes to conflicting results across studies and motivates a standardized framework for characterizing and comparing energy-delivery performance. Together, these gaps have limited understanding of the spatiotemporal thermal dynamics needed to further optimize MWA energy delivery.

Two complementary tools can help close these gaps by enabling full spatiotemporal tracking and thermal-dose endpoint evaluation. First, finite-element computational modeling has been used to simulate the biophysics of MWA heating by solving the coupled electromagnetic–bioheat physics that governs ablation³³ and can predict the full spatiotemporal temperature evolution under arbitrary pulsing schemes, offering a flexible, low-cost platform for protocol exploration and a predictive tool for treatment planning. However, computational modeling rests on predetermined tissue properties and simplifying biophysical assumptions and therefore requires experimental validation. On the experimental side, gross pathology is the most common reference standard, but it provides only a final-state snapshot, cannot reveal transient dynamics, and is largely confined to ex vivo specimens, limiting its translation to in vivo settings. Magnetic resonance thermometry (MRT), in contrast, can visualize both anatomical tissue changes and the spatiotemporal temperature history during ablation. MRT provides non-invasive, real-time

temperature monitoring with high spatial resolution, and MRT-derived thermal dose can serve as a quantitative endpoint for delineating the ablation zone²⁶. MRT can thus both validate computational models and, in principle, quantitatively evaluate energy-delivery strategies in vivo. The feasibility of a joint modeling–MRT approach has been established for characterizing transient spatiotemporal thermal effects under continuous heating⁶⁷; however, this joint approach has not yet been applied to evaluate and compare energy-delivery strategies.

The objective of this chapter is to develop and evaluate a joint computational–experimental framework combining computational modeling, MR thermometry (MRT), and gross pathology to characterize and compare the spatiotemporal thermal effects of continuous and pulsed MWA energy-delivery protocols in ex vivo liver.

2.2 Methods

2.2.1 Computational model

The microwave ablation model was implemented using the finite-element method (FEM) on a two-dimensional axisymmetric domain in COMSOL Multiphysics (v6.2, COMSOL Inc., Burlington, MA). The model couples electromagnetic wave propagation in tissue with the Pennes bioheat-transfer equation, incorporates temperature-dependent dielectric and thermal tissue properties, and outputs the full spatiotemporal temperature field $T(r, z, t)$ for a specified antenna geometry and energy-delivery protocol (continuous or pulsed). An overview of the computational model is shown in **Figure 2-1**.

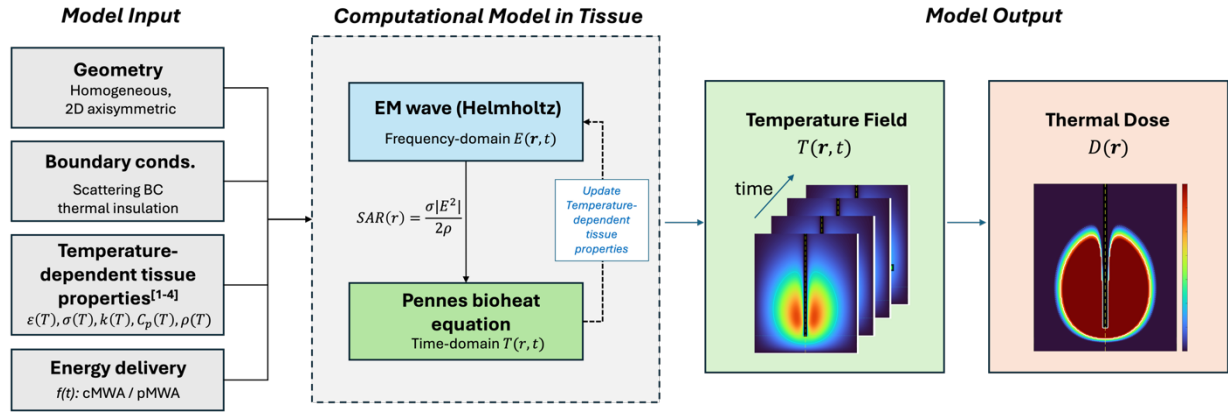


Figure 2-1. Overview of the computational modeling framework, from model inputs to temperature field and thermal dose outputs. ϵ : relative permittivity; σ : electrical conductivity; k : thermal conductivity; C_p : heat capacity; ρ : tissue density.

Model geometry and antenna design

The microwave antenna was modeled as a single-slot coaxial design (**Figure 2-2**), comprising a coaxial cable with PTFE insulation and a single air slot. The surrounding ex vivo porcine liver was represented as a uniform cylindrical domain.

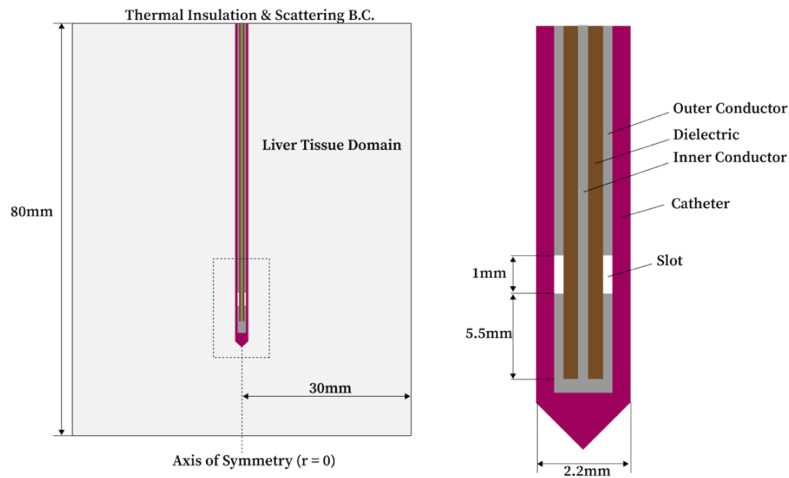


Figure 2-2. Computational model geometry and antenna design. (Left) Axisymmetric simulation domain with the antenna inserted along the symmetry axis. (Right) Zoomed-in view of the dashed region on the left, showing the coaxial slot antenna structure.

Governing equations

The time-harmonic electric field in tissue was computed from the Helmholtz (vector wave) equation,

$$\nabla \times \mu_r^{-1}(\nabla \times E) - \delta_0^2 \left(\epsilon_r - \frac{j\sigma}{\omega\epsilon_0} \right) E = 0 \quad (2-1)$$

where E is the electric field, μ_r the relative permeability (≈ 1 for biological tissue), k_0 the free-space wavenumber, ϵ_r the relative permittivity, σ the electrical conductivity, ω the angular frequency ($2\pi \times 2.45$ GHz), and ϵ_0 the free-space permittivity.

The volumetric microwave power deposited in tissue was quantified by the specific absorption rate (SAR),

$$SAR = \frac{\sigma|E|^2}{2\rho} \quad (2-2)$$

where ρ is the tissue density and $|E|$ the electric-field magnitude.

The tissue temperature field was governed by the Pennes bioheat equation,

$$\rho c_p \frac{\partial T}{\partial t} = \nabla \cdot (k \nabla T) + \rho_b c_b \omega_b (T_b - T) + Q_{ext} \quad (2-3)$$

where ρ and c_p are the tissue density and specific heat, k the thermal conductivity, and Q_{ext} the external microwave heat source; the perfusion term (subscript b) is a heat sink that was set to zero ($\omega_b = 0$) for the ex vivo condition.

The microwave heat source depends on the delivery protocol. For continuous delivery the electromagnetic and bioheat fields are fully coupled, so the source equals the local SAR scaled by tissue density and updates as the properties change with temperature:

$$Q_{ext}(\mathbf{r}, t) = \rho \cdot SAR(\mathbf{r}, T) \quad (2-4)$$

For pulsed delivery the EM field is solved once at a nominal power, and the resulting $SAR_{nominal}(r)$ is modulated by a time-dependent pulse function $f(t)$:

$$Q_{ext}(r, t) = \rho \cdot SAR_{nominal}(r) \cdot f(t) \quad (2-5)$$

Boundary conditions

EM boundary conditions comprised axial symmetry along the antenna axis, a perfect-electric-conductor condition on metallic antenna surfaces, and a scattering boundary condition on the outer domain to approximate an open region^{33,68}. Thermal boundary conditions used an initial tissue temperature of 20 °C (consistent with the ex vivo experiments), thermal insulation on the outer boundary (no heat escape), and convective cooling along the antenna shaft to represent the water-cooling circuit.

Temperature-dependent tissue properties

Liver dielectric and thermal properties were modeled as temperature-dependent to capture water-vaporization effects during heating: the relative permittivity and effective conductivity follow sigmoidal desiccation curves⁶⁸⁻⁷⁰, while the thermal conductivity, specific heat, and density follow piecewise functions across the ~100 °C vaporization transition⁴⁹ (**Table 2-1**). Power

reaching the antenna input port was scaled by a cable transmission efficiency of $\eta = 40\%$ (60% cable loss)⁷¹.

Table 2-1. Temperature-dependent tissue properties used in the computational model. ϵ_r and σ_{ef} follow sigmoidal functions of temperature; k , C_p , and ρ follow piecewise functions across the water-vaporization transition.

Property (units)	Temperature-dependent form
Relative permittivity (–)	$\epsilon_r(T) = 48.391 \cdot \left(1 - \frac{1}{1 + \exp(0.764 \cdot (82.271 - T))}\right) + 1$
Effective conductivity ($S \cdot m^{-1}$)	$\sigma_{ef}(T) = 2.173 \cdot \left(1 - \frac{1}{1 + \exp(0.697 \cdot (85.375 - T))}\right)$
Thermal conductivity ($W \cdot m^{-1} \cdot K^{-1}$)	$k(T) = \begin{cases} 0.512 & 20^\circ C \leq T < 90^\circ C \\ 0.2027 \cdot T - 17.933 & 90^\circ C \leq T < 100^\circ C \\ 0.0053 \cdot T^2 - 1.727 \cdot T + 64.681 & 100^\circ C \leq T < 113^\circ C \\ 0.5776 & T \geq 113^\circ C \end{cases}$
Specific heat capacity ($J \cdot kg^{-1} \cdot K^{-1}$)	$C_p = \begin{cases} 3600 & 20^\circ C \leq T < 100^\circ C \\ 327800 & 100^\circ C \leq T < 105^\circ C \\ 2103 & T \geq 105^\circ C \end{cases}$
Density ($kg \cdot m^{-3}$)	$\rho = \begin{cases} 1050 & 20^\circ C \leq T < 100^\circ C \\ 294 & T \geq 100^\circ C \end{cases}$

Thermal dose model

Thermal dosage was calculated using the cumulative equivalent minutes at 43 °C (CEM43) model⁴⁴. A threshold of 240 CEM was used to define the ablation zone from tissue necrosis.

High-temperature MWA induces substantial tissue contraction (reported as 30–70% volumetric shrinkage in liver⁷²), such that the post-ablation gross-pathology specimen is measured in a contracted configuration while the forward model is solved on an undeformed mesh. To reconcile this geometric mismatch, a fixed anisotropic warp (~20% longitudinal, ~10% radial)

based on experimental findings^{72,73} was applied to the simulated thermal-dose boundary to approximate tissue contraction, enabling direct comparison against MRT and gross pathology.

2.2.2 MRT Processing Pipeline

Because the MWA generator is a source of electromagnetic interference (EMI), a separate set of MRI receiver coils was placed at the foot of the patient bed to serve as dedicated EMI sensors. During reconstruction, all coil elements were ranked by the ratio of their signal energy between the central and peripheral k-space regions, and the elements with the lowest ratios were designated as EMI-sensing coils while the remainder were used for imaging. Multi-coil active EMI suppression⁷⁴ was performed, followed by either inverse Fourier transform (for R=1) or GRAPPA reconstruction (for R=2) and adaptive coil combination. (Details regarding the EMI suppression method are presented in **Chapter 4**.)

PRF temperature changes were calculated using cumulative complex-conjugate PRF thermometry.

$$\Delta\phi(t) = \sum_{j=1}^t \arg(I_j \cdot I_{j-1}^*) \quad (2-6)$$

$$\Delta T(t) = \frac{\Delta\phi(t)}{\gamma \cdot \alpha \cdot B_0 \cdot TE} \quad (2-7)$$

where ΔT is the cumulative PRF temperature change at time frame t , $\arg(I_j \cdot I_{j-1}^*)$ is the conjugate phase difference between two successive dynamic complex images, γ is the gyromagnetic ratio ≈ 42.58 MHz/Tesla, α is the PRF temperature coefficient ≈ -0.01 ppm/ $^{\circ}$ C, B_0 is the main magnetic field strength, and TE is the echo time. Field drift was corrected by fitting a first-order polynomial to a non-heated reference region. Thermal dosage was calculated

using the CEM43 model with a threshold of 240 CEM to define the ablation zone. The full MRT pipeline is illustrated in **Figure 2-3**.

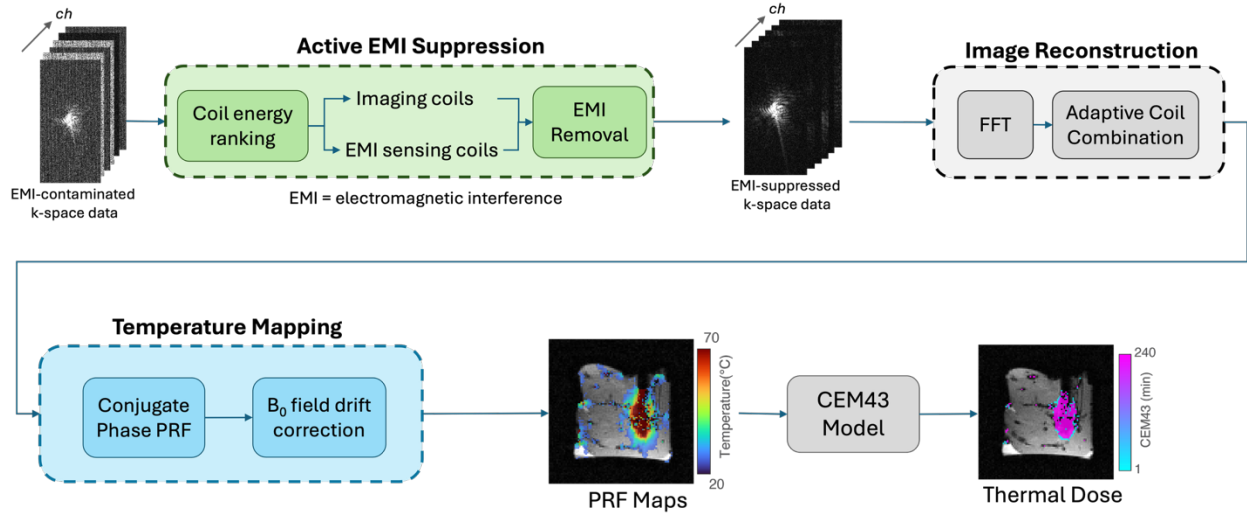


Figure 2-3. MR thermometry processing pipeline, from active EMI suppression and image reconstruction to PRF-based temperature mapping and CEM43 thermal-dose calculation.

2.2.3 MRI-guided MWA Experiments

Experiments were conducted on freshly excised porcine liver (< 2 h post-resection) using a 2.45 GHz water-cooled MWA system (Saberwave ECO-200G, Nanjing ECO Medical Instrument Co., China) and a 16-gauge MR-compatible antenna.

Three energy-delivery protocols were experimentally tested (**Figure 2-4**): (1) continuous high-power, 100 W for 4 min (24 kJ); (2) continuous lower-power, 65 W for 10 min (39 kJ) and (3) pulsed, 100 W for 10 min at a 40% duty cycle (15 s on / 20 s off; 24 kJ). Protocols (1) and (3) deliver the same total energy (24 kJ) to isolate the effect of pulsing, while protocol (2) represents a commonly used lower-power continuous regimen.

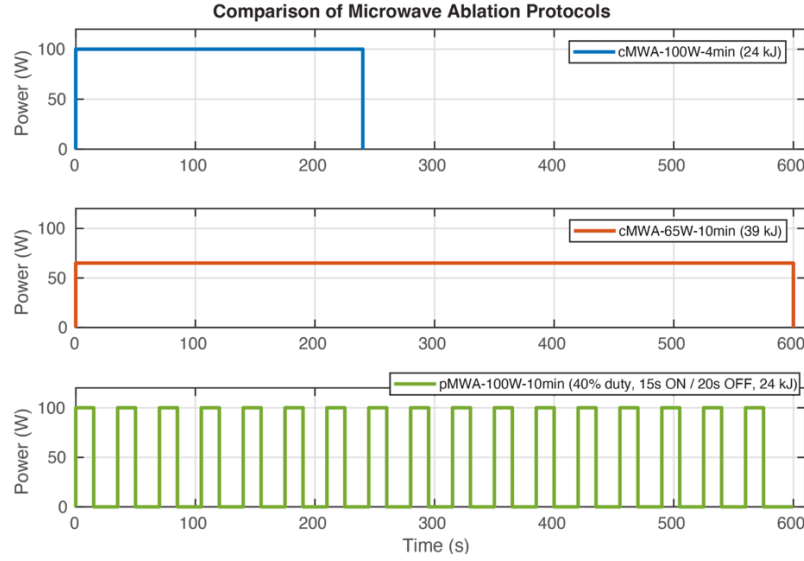


Figure 2-4. Power delivery profiles for the three microwave ablation protocols compared in this study: continuous 100 W for 4 min, continuous 65 W for 10 min, and pulsed 100 W for 10 min (40% duty cycle, 15 s on/20 s off).

MRI was performed on a 3 T scanner (Prisma, Siemens, Germany) using phased array coils.

Dynamic temperature imaging was performed with a 2D spoiled gradient-echo sequence (TR/TE = 16/11.52 ms, flip angle = 8°, FOV = 277×180 mm², matrix = 96×148, slice = 3 mm, temporal resolution = 2.36 s/frame). After ablation, tissues were dissected along the antenna tract for gross evaluation.

2.2.4 Evaluation

To validate the FEM-based computational model and the MRT processing pipeline, the coagulation zone from ex vivo gross pathology (AZ-GT) was used as the reference ablation zone. The coagulation zone was defined as necrotic tissue with irreversible thermal damage—the

“white zone”. Its boundary was manually annotated in 3D Slicer, with pixel spacing calibrated against a known reference distance. The gross-pathology reference (AZ-GT) was compared with the ablation zones from computational modeling (AZ-model) and MRT (AZ-MRT), both defined by the CEM43 model with a threshold of 240 minutes. Agreement was quantified by the Dice similarity coefficient (DSC), long- and short-axis diameters, circularity, and area.

2.3 Results

2.3.1 MRT Validity

Before comparing simulation with MRT, the accuracy of the MRT measurements was verified against fiber-optic temperature probes during a continuous MWA protocol. MRT achieved a temperature accuracy of 2.8 °C relative to the probe reading in the heated region and a stability of 1.7 °C in a non-heated reference region (**Figure 2-5**).

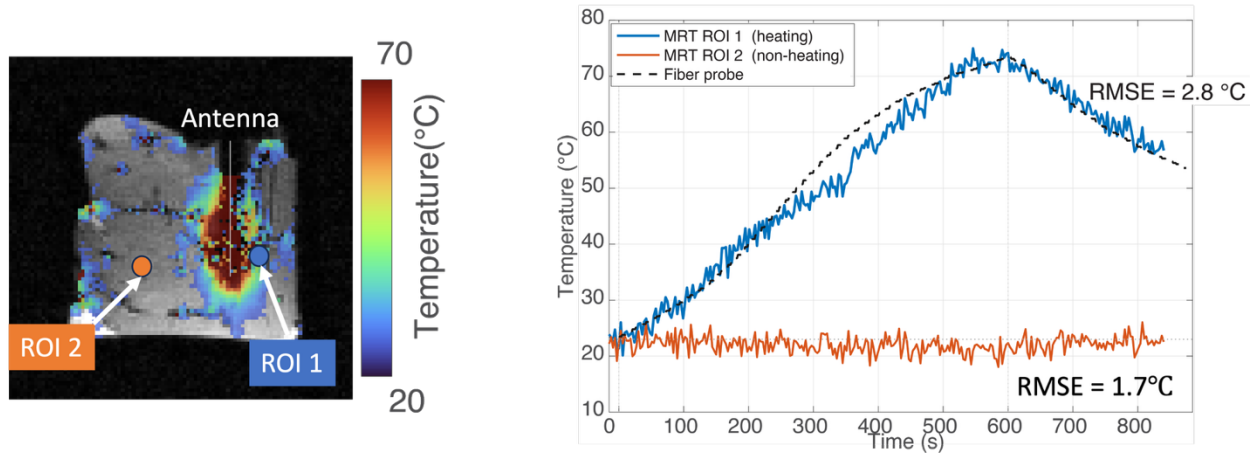


Figure 2-5. Validation of MR thermometry against fiber-optic temperature probes. Left: representative PRF-based temperature map with ROI 1 (heating zone, near antenna) and ROI 2 (non-heating background). Right: temperature-time curves from MRT versus fiber-optic probe measurements at the corresponding ROIs, showing good agreement between the two modalities (RMSE = 2.8 °C for ROI 1, 1.7 °C for ROI 2).

Real-time MRT successfully resolved the transient thermal behavior during pulsed delivery. The magnitude images showed periodic signal changes consistent with water-vapor formation and fluid inflow/outflow with each pulse; the PRF temperature maps revealed periodic expansion and contraction of the heated region between pulses; and the CEM43 thermal-dose maps showed that, despite intermittent heating, thermal dose accumulated progressively across successive pulses, yielding a clearly delineated ablation boundary.

2.3.2 Computational Modeling Validity

The ablation zone predicted by the computational model was evaluated against the coagulation zone from ex vivo gross pathology. The model was implemented in COMSOL Multiphysics and executed through LiveLink for MATLAB, with post-processing performed in MATLAB. The model was validated against two ex vivo tissue specimens. The predicted ablation zone agreed well with gross pathology, achieving a DSC of 0.944 and a 95th-percentile Hausdorff distance (HD95) of 1.6 mm for the 65 W $\times$ 10 min protocol.

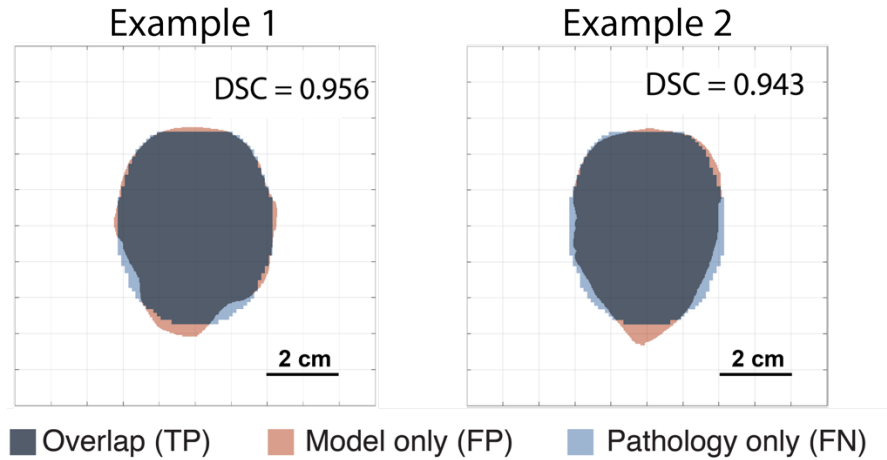


Figure 2-6. Computational model validation against gross pathology. Representative examples showing spatial overlap between the simulated and pathology-derived ablation-zone boundaries, with overlap (true positive, TP), model-only (false positive, FP), and pathology-only (false negative, FN) regions indicated for two representative cases. Model and pathology boundaries show strong agreement (DSC = 0.956 and 0.943).

2.3.3 Computational Modeling vs. MRT

Direct comparison of 2D temperature maps between MRT and computational modeling under the pulsed protocol (**Figure 2-7**) showed overall agreement in the spatial temperature distribution, shape, and pulsing rate. MRT maps exhibited susceptibility-related artifacts and noise, whereas the computational model produced a smoother temperature field, but the overall spatiotemporal pattern matched well.

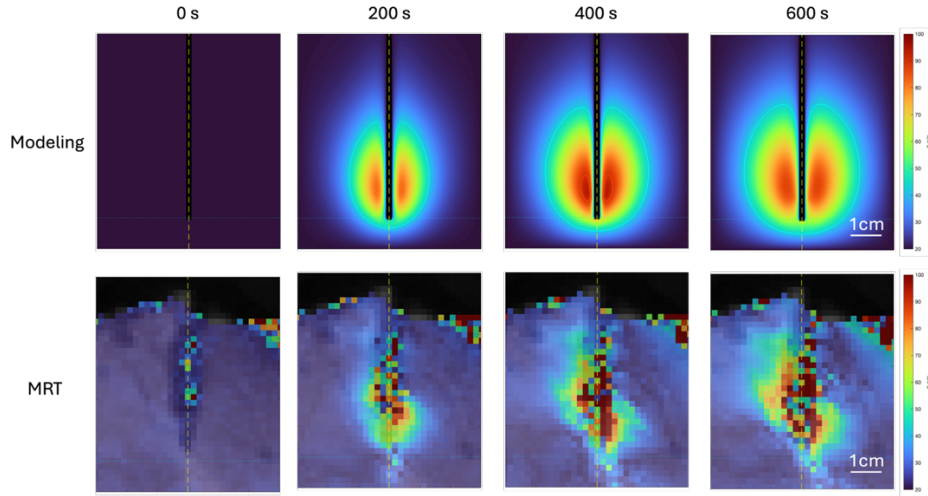


Figure 2-7. Transient temperature field comparison between computational modeling and MR thermometry using the pulsed 100 W MWA protocol. Simulated (top) and MRT-measured (bottom) temperature fields are shown at 0, 200, 400, and 600 s, illustrating the spatial growth of the heated region around the antenna over the course of ablation. Modeled and measured temperature distributions show consistent spatial patterns throughout treatment.

Temperature-evolution curves extracted from an ROI 10 mm from the antenna axis showed good agreement between MRT (solid lines) and simulation (dashed lines) across all three protocols (**Figure 2-8**), with RMSE ranging from 4.4 to 8.9 °C. The 100 W $\times$ 4 min protocol showed the largest discrepancy, potentially reflecting more severe susceptibility artifacts from water-vapor formation at very high temperatures. The pulsed protocol exhibited a slower temperature rise with periodic fluctuations corresponding to the duty cycle.

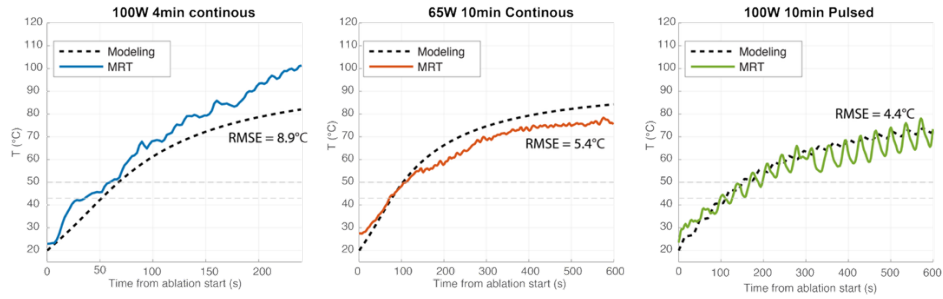


Figure 2-8. ROI-based temperature evolution comparison between computational modeling and MR thermometry across all three protocols. Simulated and MRT-measured temperature-time curves within the heating ROI are shown for continuous 100 W/4 min (left), continuous 65 W/10 min (middle), and pulsed 100 W/10 min (right), with RMSE = 8.9, 5.4, and 4.4 °C, respectively.

2.3.4 Ablation-zone geometry: modeling vs. MRT vs. gross pathology

Ablation-zone geometry was compared across modeling, MRT, and gross pathology for the three protocols (**Figure 2-9**). The simulated CEM43 thermal-dose maps slightly overestimated ablation-zone size relative to gross pathology in all three protocols, but both modalities captured the same overall trends: the high-power continuous protocol produced the most elongated zone, while the lower-power continuous protocol produced the largest overall ablation zone.

Quantitative measurements are summarized in **Table 2-2** and **Figure 2-10**.

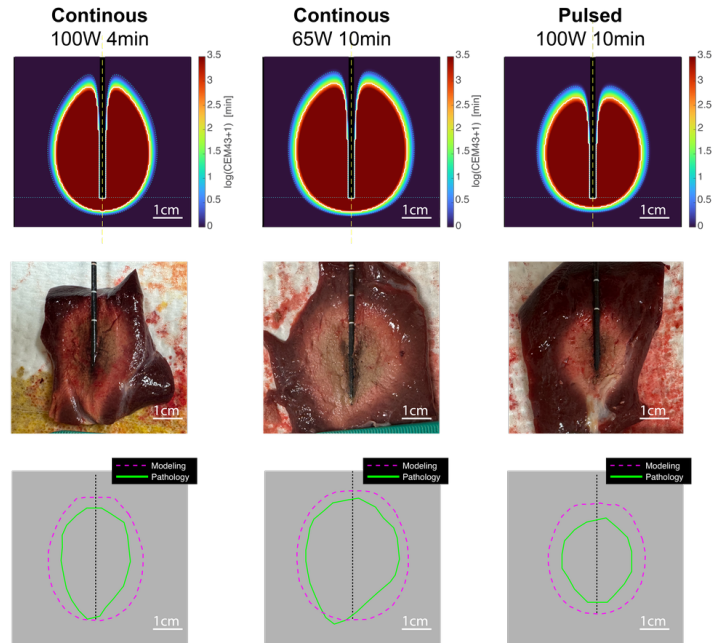


Figure 2-9. Ablation-zone geometry across the three MWA protocols, comparing computational modeling and gross pathology. Simulated CEM43 thermal-dose maps (top), gross-pathology specimens (middle), and boundary overlays of modeled versus pathology-derived ablation zones (bottom) are shown for continuous 100 W/4 min, continuous 65 W/10 min, and pulsed 100 W/10 min protocols. The simulation slightly overestimates ablation-zone size relative to pathology but reproduces the overall trends across protocols.

Table 2-2. Quantitative ablation-zone geometry (long-axis and short-axis diameters, circularity, and area) measured from computational modeling, MR thermometry (MRT), and gross pathology for the three protocols.

	Continuous 100 W × 4 min			Continuous 65 W × 10 min			Pulsed 100 W × 10 min (40%)		
Metric	Model	MRT	Path.	Model	MRT	Path.	Model	MRT	Path.
Long axis, LA (mm)	41.2	39.6	33.9	42.7	37.5	37.4	36.4	40.8	29.9
Short axis, SA (mm)	32.1	28.3	24.1	37.4	35.9	33.3	32.8	30.1	27.0
Circularity (SA/LA)	0.78	0.72	0.71	0.88	0.96	0.89	0.90	0.74	0.90
Area (mm²)	1078.4	891.2	619.4	1339.5	1209.8	963.1	994.4	787.4	500.2

2.3.5 Gross pathology and ablation-zone circularity

Quantitative geometry confirmed these observations (**Table 2-2**, **Figure 2-10**). The high-power continuous protocol ($100\text{ W} \times 4\text{ min}$) yielded the lowest circularity ($0.71\text{--}0.78$ across modalities), consistent with an elongated, tear-drop-shaped lesion, whereas the lower-power continuous ($65\text{ W} \times 10\text{ min}$) and pulsed ($100\text{ W} \times 10\text{ min}$, 40% duty) protocols produced rounder zones (circularity $\approx 0.74\text{--}0.96$). The lower-power continuous protocol produced the largest ablation-zone area.

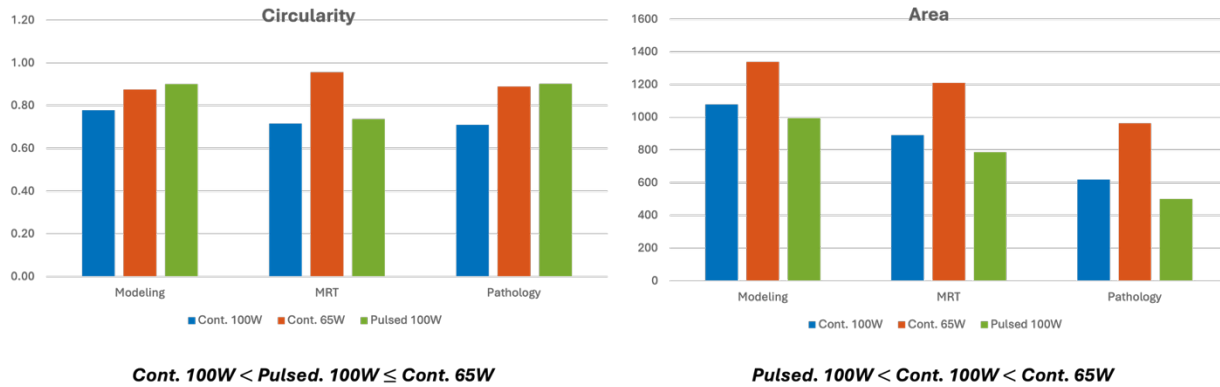


Figure 2-10. Quantitative comparison of ablation-zone circularity and area across modeling, MRT, and gross pathology for the three protocols, corresponding to **Table 2-2**. Circularity was comparable across modalities and protocols, while modeled and MRT-measured ablation-zone area consistently exceeded pathology measurements, with the continuous 65 W protocol producing the largest area across all three modalities.

2.4 Discussion

In this chapter, we combined real-time MRT and computational modeling to characterize the spatiotemporal thermal effects of continuous and pulsed MWA in fresh ex vivo porcine liver.

MRT captured the transient dynamics unique to pulsed delivery — cyclic cooling–reheating, fluid inflow/outflow, and progressive thermal-dose accumulation — and a coupled EM–bioheat

model reproduced the near-field temperature evolution and the overall ablation-zone geometry across protocols, with quantifiable discrepancies that point to specific opportunities for model refinement.

To our knowledge, this is among the first uses of real-time MRT to characterize the thermal dynamics of pulsed MWA. MRT resolved individual pulsing cycles and the associated expansion–contraction of the heated region, and the CEM43 dose maps tracked the progressive growth of the ablation zone despite intermittent heating. This demonstrates the value of MRT for non-invasively monitoring tissue response, treatment progression, and ablation-boundary delineation during MRI-guided MWA, and it provides a quantitative endpoint (thermal dose) for evaluating energy-delivery strategies.

Validated against MRT, the computational model showed good temperature fidelity in the near-field region of the antenna across all three protocols, indicating that the dominant EM and bioheat interactions close to the energy source were well captured. The model also solved quickly (~2 min per protocol in the forward direction), making it practical for protocol exploration. However, agreement degraded at the far-field ablation boundary, particularly for the pulsed protocol, where the analysis indicated short-axis discrepancies as large as ~40% and the geometry comparison showed a consistent overestimation of ablation-zone size. These discrepancies suggest that model assumptions adequate for steady energy delivery may not fully capture the complex cooling–reheating dynamics and may misestimate thermal diffusion in the far field. Incorporating additional temperature-dependent properties, thermal hysteresis, and dynamic perfusion — together with refined MRT processing — may improve fidelity at the

ablation boundary, which is critical for ensuring adequate safety margins around critical structures.

This work demonstrates a joint computational–experimental approach that leverages the complementary strengths of each modality: modeling provides a flexible, low-cost environment for testing biophysical parameters and protocols, while MRT directly measures the realistic thermal response in tissue, including effects such as perfusion and heterogeneity that are difficult to model *a priori*. Combined with post-ablation gross pathology, this modeling–MRT–pathology workflow forms a multimodal framework for evaluating MWA energy-delivery strategies. Such a framework has translational potential to inform patient-specific treatment planning, to support prospective optimization of energy delivery, and ultimately to enable temperature-feedback control for safer, more predictable ablation.

This study has several limitations. The experiments were conducted *ex vivo* and therefore did not capture *in vivo* factors such as active blood perfusion, large-vessel heat-sink effects, and tissue anatomical heterogeneity; MRT is, however, directly translatable to *in vivo* settings, providing a path toward *in vivo* validation. The pulsed protocol was controlled manually, which may have introduced minor deviations from the ideal pulse timing. The model–experiment discrepancies, particularly for pulsed delivery, indicate that the tissue-property parameters require further calibration against experimental data. Future work will focus on calibrating the model parameters, refining the MRT processing pipeline, extending the analysis to a broader range of pulsing parameters, and progressing toward *in vivo* validation.

2.5 Conclusion

This chapter presents one of the first uses of MR thermometry to characterize the spatiotemporal thermal dynamics of pulsed MWA and to validate a computational model under intermittent energy delivery. By capturing transient cooling–reheating behavior and progressive thermal-dose accumulation, and by comparing model predictions against both MRT and gross pathology, this joint computational–experimental approach establishes a foundation for further model calibration and for the optimization of MWA energy-delivery strategies toward safer and more predictable ablation.

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CHAPTER 3 VOLUMETRIC THERMOMETRY IN MOVING TISSUES USING STACK-OF-RADIAL MRI AND AN IMAGE-NAVIGATED MULTI-BASELINE PRF SHIFT TECHNIQUE

3.1 Introduction

Thermal ablation is an increasingly utilized strategy for treating primary early-stage liver tumors by raising the local tumor temperature to cytotoxic levels (above 50–60 °C)⁷⁵. Common energy sources for ablation include laser⁷⁶, high-intensity focused ultrasound (HIFU)⁷⁷, radiofrequency currents¹², and microwave fields¹⁴. Thermal ablation is performed via minimally invasive approaches under image guidance and is considered the preferred approach for candidates not suitable for surgical resection¹¹. The technical success of thermal ablation procedures is highly dependent on reliable intra-procedural imaging for both guidance and monitoring to ensure treatment efficacy and safety.

Current standard imaging techniques for intra-procedural characterization of ablation include real-time ultrasound⁷⁸ and CT imaging⁷⁹, both of which track microbubble formation from water vapor during ablation. These microbubbles serve as a surrogate marker for the temperature distribution within the ablation zone. However, directly correlating microbubble formation to actual temperatures is challenging, which complicates the assessment of whether the ablation margin is sufficient to effectively treat the tumor^{10,11}. Furthermore, it is unclear how close the ablation zone can approach critical structures, such as blood vessels or the liver capsule, before risking irreversible damage^{10,11}.

Magnetic resonance (MR) thermometry^{25,26} is a powerful modality for monitoring thermal ablation. It provides non-invasive temperature mapping, enabling monitoring and prediction of heat-induced tissue death and prevention of thermal damage to surrounding critical structures. Among various MR parameters sensitive to temperature change, the proton resonance frequency shift (PRF)-based thermometry method^{80,81} is the most widely used. The resonance frequency of water protons decreases linearly with increasing temperature (approximately -0.01 ppm/ $^{\circ}\text{C}$)^{80,81}, a relationship that is largely tissue-independent (except for adipose tissues, which lack hydrogen bonds). PRF thermometry has been successfully applied in monitoring liver tumor ablation using laser⁴², radiofrequency currents⁸², HIFU⁸³, and microwave therapies⁵², and has been adopted clinically for MR-guided minimally invasive transcranial procedures⁸⁴, and for the treatment of localized breast¹⁷ and prostate cancers¹⁹, bone metastases²⁸, and uterine fibroids²⁷.

Despite the technical feasibility and promise, PRF thermometry faces significant challenges for monitoring liver tumor ablation, as the presence of respiratory motion can cause artifacts that confound temperature measurements⁸⁵. Errors associated with intra-scan motion can be partially mitigated using fast imaging sequences, such as single-shot or segmented 3D echo-planar imaging (EPI), or by implementing respiratory gating/triggering⁵². Inter-scan motion-induced PRF temperature errors can be addressed using a multi-baseline approach^{42,50}, where a library of baseline images at different motion positions is acquired prior to heating. During treatment, these baseline images can be compared with the incoming dynamic images based on the motion position derived from methods such as navigator echoes⁸⁶ or optical flow⁸⁷ to obtain a matched baseline image for calculating PRF thermometry. A recent review summarized common techniques for mitigating motion-induced temperature artifacts⁸⁸.

While the combination of fast imaging sequences and the multi-baseline PRF approach has reduced motion-induced temperature errors, most prior work has been limited to acquiring a single 2D slice or a few 2D slices^{50,86,87,89,90}. This limitation represents a tradeoff between spatiotemporal resolution, volumetric coverage, and signal-to-noise ratio (SNR). In general, these constraints have restricted the ability of prior PRF methods to monitor a volume that encompasses the full tumor, 5-10 mm safety margins in all directions, and surrounding critical structures over the relevant range of respiratory motion. For effective monitoring of liver ablation procedures, achieving sufficient volumetric coverage is essential to ensure a complete ablation to prevent local tumor recurrence and avoid thermal injury to critical structures.

Non-Cartesian MR acquisition techniques, such as stack-of-radial MRI, offer a promising solution for monitoring ablation in moving tissues. Radial trajectories are inherently robust to motion due to their sampling geometry and repeated sampling of the k-space center⁹¹. Additionally, the golden-angle-ordered radial sampling strategy³⁸ enables flexible reconstruction of dynamic images by re-grouping of the data, allowing optimization of spatiotemporal resolution to improve volumetric coverage. Two radial reconstruction techniques, k-space-weighted image contrast (KWIC) filter^{39,92} and Golden-angle RAdial Sparse Parallel (GRASP) MRI⁹³, are particularly suited for dynamic volumetric thermometry. KWIC reconstruction balances between effective temporal resolution and image fidelity by combining low-frequency k-space data from a narrow temporal window and high-frequency data from a broader temporal window. KWIC reconstruction has been explored for volumetric PRF thermometry in static tissues and scenarios with limited motion^{40,41}, but its performance in tissue undergoing continuous respiratory motion remains underexplored. GRASP reconstruction, on the other hand, exploits temporal sparsity and solves an optimization problem to reconstruct images from highly

undersampled data. While GRASP has been applied in various free-breathing dynamic volumetric MRI applications⁹³⁻⁹⁵, it has not yet been investigated in MR thermometry.

In this study, we propose a novel volumetric MR thermometry framework for monitoring thermal ablation in moving tissues, combining a golden-angle-ordered stack-of-radial MRI sequence with an image-navigated multi-baseline (iNAV-MB) PRF method. The iNAV-MB method enables direct motion estimation from the reconstructed dynamic magnitude images, facilitating motion-compensated PRF temperature mapping. We implement and adapt two radial MRI reconstruction methods, KWIC³⁹ and GRASP⁹³, with a sliding window-based reconstruction approach for volumetric PRF thermometry. We compare KWIC + iNAV-MB and GRASP + iNAV-MB, as well as both KWIC and GRASP paired with conventional single-baseline PRF thermometry, to evaluate their performance in measuring temperature changes during motion. The proposed framework is evaluated through an ex vivo tissue HIFU ablation study using a programmable motion phantom and in vivo non-heating swine experiments.

3.2 Methods

3.2.1 Overall Framework for Volumetric PRF Thermometry

De Senneville et al. have previously discussed the general requirements for MR temperature mapping in monitoring thermal ablation²⁶. To obtain reliable volumetric thermometry in tissues experiencing respiratory motion (such as liver and kidney), several additional requirements should be met: (1) a field of view (FOV) with sufficient volumetric coverage to capture most early-stage tumors, target margin, and surrounding critical structures, (2) high effective temporal resolution to resolve intra-frame motion caused by respiration, (3) robust motion compensation

techniques to address inter-frame motion, and (4) minimal imaging artifacts arising from undersampling and motion effects within the tissue of interest. These considerations guided the development and evaluation of our proposed framework.

The overall framework is presented in **Figure 3-1**. Data acquisition was performed using a golden-angle-ordered 3D stack-of-radial MRI sequence. This stream of radial k-space data was reconstructed using a sliding window approach to form volumetric image frames with narrow temporal windows (i.e., high effective temporal resolution < 1 second per volume). To achieve a narrow temporal window, each volumetric image frame required a high data undersampling factor compared to the Nyquist criteria (**Figure 3-1A**). Two dynamic radial MRI reconstruction techniques, KWIC and GRASP, were employed and compared. The reconstructed 3D magnitude images (axial volume) were reformatted into the coronal orientation, where image-based motion navigation was used to extract a motion signal curve along the superior-inferior (S/I) direction (**Figure 3-1C**). The reconstructed 3D phase images, combined with the extracted iNAV signals, were used to perform image-navigated multi-baseline (iNAV-MB) PRF thermometry, generating motion-compensated 3D dynamic temperature maps (**Figure 3-1D**).

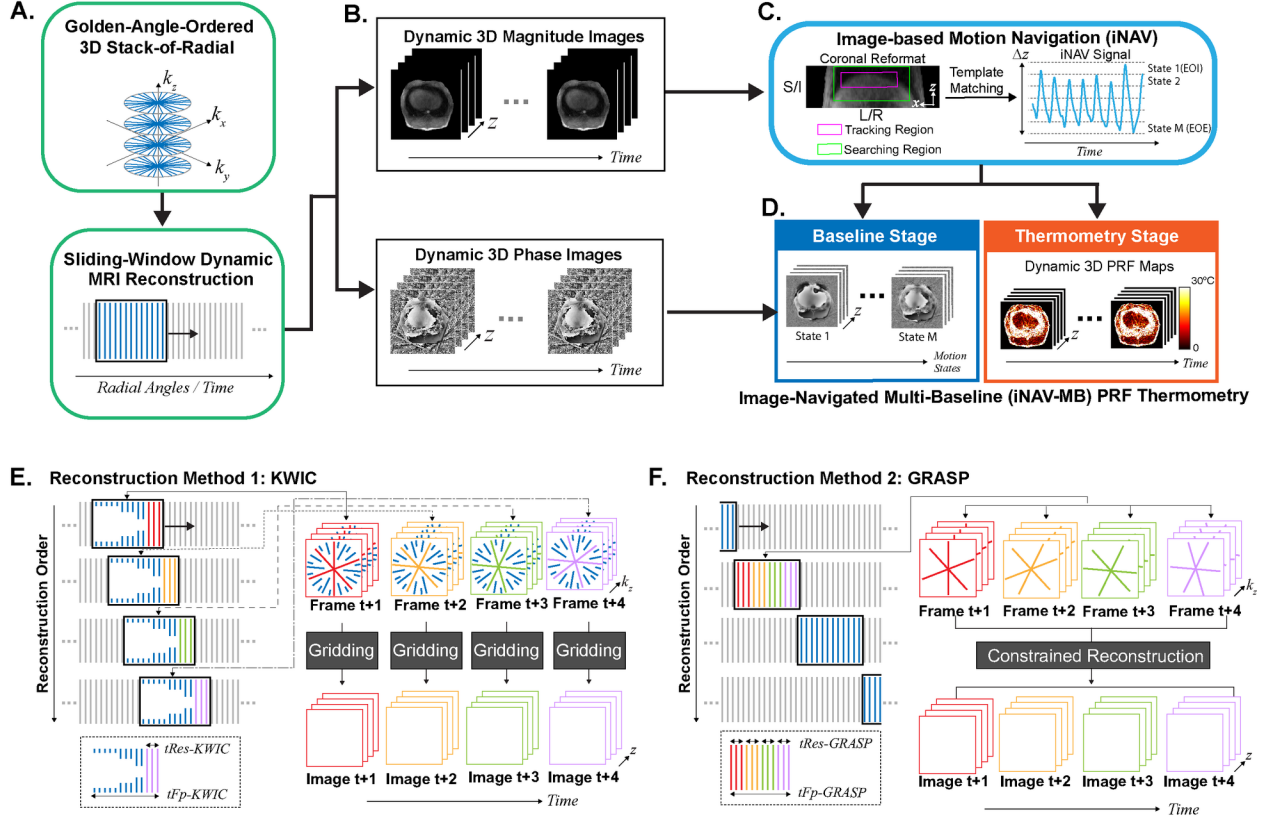


Figure 3-1. An overview of the proposed volumetric PRF thermometry framework. **(A)** The acquired dynamic multi-echo golden-angle 3D stack-of-radial data is reconstructed with a sliding-window approach. **(B-D)** The reconstructed dynamic magnitude images are used to obtain the image-based motion navigation (iNAV) signal. A multi-baseline library is formed using the images from the baseline stage and the extracted iNAV signal. During the thermometry stage, the PRF temperature map at each time point is calculated with dynamic motion compensation (details are illustrated in **Figure 3-2**). **(E-F)** Diagrams of the two dynamic reconstruction methods used in this work. Their effective temporal resolutions (tRes) and temporal footprints (tFp) are defined in the diagram and the text. EOE: end-of-expiration; EOI: end-of-inspiration; PRF: proton resonance frequency shift; KWIC: k-space weighted image contrast; GRASP: golden-angle radial sparse parallel MRI.

3.2.2 Golden-Angle-Ordered 3D Stack-of-Radial Sequence

A 3D stack-of-radial multi-echo spoiled gradient-echo MRI sequence^{40,96} was used. The sequence used radial sampling in the k_x and k_y directions and Cartesian sampling along the slice-encoding (k_z) direction. A bipolar multi-echo readout gradient was used to acquire the multi-

echo data. Radial data were first acquired along the slice-encoding direction (k_z), using spokes with the same azimuthal angle, and subsequent radial data were acquired with an increment of a constant azimuthal angle of 111.25° derived from the golden ratio³⁸. This sampling scheme enables flexible adjustment of effective temporal resolution during the reconstruction of dynamic image frames. A multi-echo acquisition was used to improve image SNR⁴¹ and enhance tissue boundary contrast⁹⁷ for iNAV motion tracking (as described in Section 3.2.4). Prior to image reconstruction, the multi-channel radial k-space data were pre-whitened⁹⁸ and corrected for gradient delays⁹⁶. An inverse Fourier transform was applied along the k_z direction to produce a set of 2D radial k-space datasets corresponding to the multiple slices for subsequent reconstruction. Reconstructed dynamic 3D images were coil-combined using adaptive coil combination⁹⁹. The multi-echo⁹⁹ magnitude images at each time point were echo-combined using sum-of-squares for iNAV motion tracking, and the last echo phase image at each time point was used for PRF temperature mapping.

3.2.3 Dynamic Radial MRI Reconstruction

KWIC reconstruction

KWIC reconstruction uses radial k-space data efficiently by including adjacent radial k-space data from a larger temporal window for reconstruction, balancing between motion consistency and data undersampling. To capture the most recent information and minimize the temporal delay, a backward-looking asymmetric KWIC filter^{40,100} was implemented. For each KWIC reconstruction window, the innermost k-space region contains only the most recently acquired radial data from a narrow temporal window while the outer k-space is filled with data from

previously sampled radial k-space data from a larger temporal window. Motion consistency is preserved because the central k-space region contains data from a small acquisition window. The effective temporal resolution of the KWIC reconstruction window ($tRes-KWIC$) is defined as the time required to acquire the innermost k-space region from all k_z encodings^{39,41}, while the temporal footprint ($tFp-KWIC$) corresponds to the time required to acquire all radial data within a KWIC reconstruction window from all k_z encodings^{40,100,101}. The choice of effective temporal resolution ($tRes-KWIC$) and temporal footprint ($tFp-KWIC$) is optimized for motion tracking capability by lowering $tRes-KWIC$ and $tFp-KWIC$, as recommended by Svedin et al.¹⁰⁰, while still maintaining a desired volumetric coverage and sufficient SNR. The effective temporal resolution of KWIC reconstruction ($tRes-KWIC$) was chosen to be around 1 second per volume to resolve respiratory motion (around 3-5 seconds/breath), and the temporal footprint of KWIC reconstruction ($tFp-KWIC$) was chosen to be around 10 seconds. 2D re-gridding¹⁰² with density compensation¹⁰³ was used for image reconstruction for each KWIC reconstruction window. The KWIC reconstruction window was advanced with a temporal step size that equals the number of radial angles filling the innermost k-space region (**Figure 3-1E**).

GRASP reconstruction

GRASP reconstruction uses a compressed sensing framework with temporal sparsity constraints to handle highly undersampled radial data. Originally designed for dynamic contrast-enhanced MRI, GRASP typically reconstructs data from the entire course of temporal contrast changes after the acquisition is completed. To adapt GRASP for dynamic temperature mapping, which requires continuously updated reconstruction results during a procedure for monitoring, we implemented a sliding-window approach for GRASP to minimize the temporal delay,

reconstructing only a few temporal frames at a time. For each GRASP reconstruction window, a total variation constraint was applied along the temporal dimension and the following optimization problem was solved:

$$\hat{m} = \underset{m}{\operatorname{argmin}} \|F \cdot S \cdot m - d\|_2^2 + \lambda \|T \cdot m\|_1 \quad (3-1)$$

where F is the non-uniform Fast Fourier Transform operator, S is the coil sensitivity maps, m is the current set of dynamic 3D images to be reconstructed, d is the acquired multi-echo multi-channel 3D k-space data, λ is the regularization parameter, and T is the temporal total variation operator. The effective temporal resolution of each frame in the GRASP reconstruction window ($tRes-GRASP$) was defined as the time required to acquire radial angles from one temporal frame along all k_z encoding steps, and the temporal footprint of each GRASP reconstruction window ($tFp-GRASP$) was the time needed to acquire all radial angles within the reconstruction window. $tRes-GRASP$ and $tFp-GRASP$ were matched to those of KWIC reconstruction for comparison. The regularization parameter was determined using a grid search⁹³ to achieve a balance between the motion averaging effects near tissue/air boundaries and radial undersampling artifacts. Coil sensitivity maps were estimated using radial data acquired during a non-heating baseline stage. After each reconstruction step, the GRASP reconstruction window was advanced without overlapping with the previous one, using a temporal step size equal to the entire GRASP reconstruction window (**Figure 3-1F**). Both KWIC and GRASP reconstruction methods were performed offline using MATLAB R2021a (MathWorks, Natick, MA).

3.2.4 Image-Navigated Multi-Baseline PRF Thermometry

iNAV-MB PRF thermometry combined image-based motion tracking with multi-baseline phase processing to minimize motion-induced temperature errors. Magnitude images were used to estimate tissue displacement Δz along the S/I direction at a timepoint t using a template matching algorithm¹⁰⁴. A rectangular region-of-interest (ROI) containing prominent tissue features (e.g., liver dome) was manually selected on a reference frame as the template for tracking, while a broader region that encompasses potential motion trajectories, as shown in **Figure 3-1C**, was automatically designated as the search region in subsequent image frames. The reference frame was specified to be a frame near the most stable motion position, for example, the end-of-expiration (EOE) position for the liver, during the non-heating baseline stage. iNAV motion tracking was then performed automatically using least-squares optimization to calculate the displacement of the template across time frames.

After performing iNAV processing for all image frames in the baseline stage (**Figure 3-2A**), the phase images from the baseline stage were first sorted based on their iNAV signal and binned into M motion states, where M is determined as D/u , D represents the estimated S/I motion range in the subject (e.g., 15-20 mm), and u is the slice thickness (S/I resolution of the iNAV signal). Next, the baseline phase images with the same motion state were averaged, generating an iNAV multi-baseline library containing high-quality motion-resolved baseline phase images representing each motion state (**Figure 3-2B**).

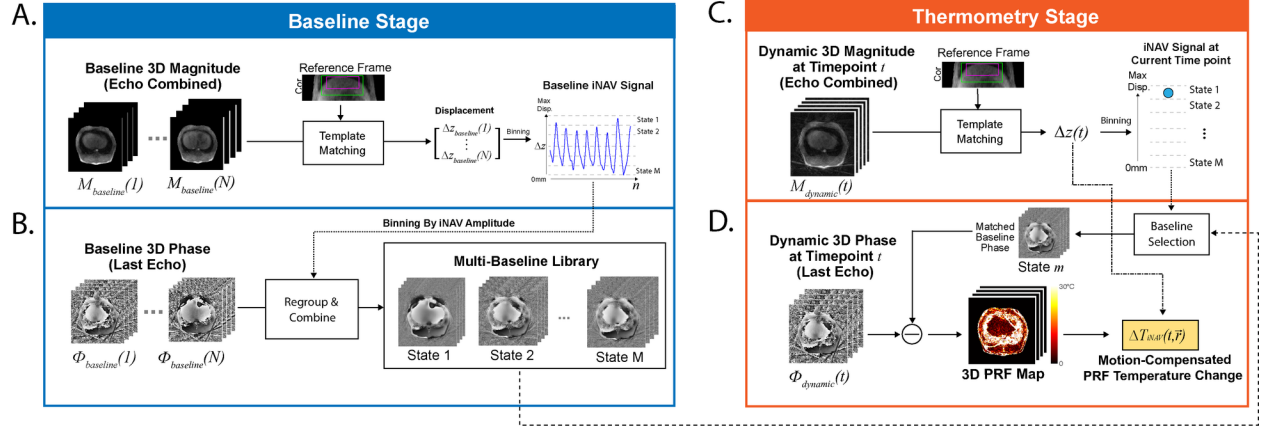


Figure 3-2. Detailed pipeline for the image-navigated multi-baseline (iNAV-MB) PRF thermometry technique. **(A)** During the baseline stage (prior to heating), the baseline magnitude images are echo-combined, and the baseline iNAV signal is extracted using a template matching algorithm. A spatial region containing the liver dome from a baseline image at the EOE position is selected as the template. **(B)** Using the iNAV signal, the baseline phase images from the last echo time are grouped and combined into different motion states and saved as a library. **(C)** During the thermometry stage, the liver displacement at each time point is calculated by comparing the incoming dynamic magnitude image to the template image. **(D)** Based on the liver displacement information, the corresponding baseline phase from the closest motion state is selected from the library and used to calculate PRF temperature maps.

During the thermometry stage, similar iNAV processing was performed to estimate the iNAV signals $\Delta z(t)$ at each timepoint t (**Figure 3-2C**). Afterward, the optimal baseline image with a similar motion position was determined for calculating PRF temperature change maps (**Figure 3-2D**). The iNAV signal $\Delta z(t)$ was additionally used for computing motion-compensated PRF temperature change (ΔT) at each voxel $\vec{r}$ using the following equation:

$$\Delta T_{iNAV}(t, \vec{r}) = \frac{\phi_d(t, \vec{r} + \Delta z(t)) - \bar{\phi}_m(\vec{r})}{\gamma \cdot \alpha \cdot B_0 \cdot TE} \quad (3-2)$$

where $\vec{r}$ is the voxel coordinate at (x, y, z) , $\bar{\phi}_m$ is the 3D phase image from the multi-baseline library ($m = 1, 2, \dots, M$), ϕ_d is the dynamic 3D phase image at each time point, γ is the gyromagnetic ratio ≈ 42.58 MHz/Tesla, α is the PRF temperature coefficient ≈ -0.01 ppm/ $^{\circ}\text{C}$, B_0 is the main magnetic field strength, and TE is the echo time. In this way, the position of any

tissue ROI within the imaging FOV can be continuously updated and compensated for each timepoint, ensuring accurate temperature monitoring in moving tissues. Field drift correction for the calculated temperature values was performed by using a first-order polynomial fit to a non-heated tissue region¹⁰⁵ followed by temporal low-pass filtering⁸⁷.

3.2.5 Ex Vivo Motion Phantom HIFU Ablation Experiment

An ex vivo porcine tissue sample (pork chop) was allowed to reach room temperature before HIFU sonication. A programmable MR-compatible motion phantom¹⁰⁶ was used to evaluate the proposed framework, as shown in **Figure 3-3**. The phantom emulated one-dimensional respiratory motion along the S/I direction using a waveform recorded from a previous human subject MRI experiment (peak-to-peak amplitude: 16 mm; respiratory period: 5.4 seconds/breath). The tissue sample was mounted on the motion platform. A research HIFU system (Image Guided Therapy, Bordeaux, France) was used. The HIFU transducer, which was fixed to the patient table, has an eight-element annular array, an operating frequency of 1.5 MHz, maximum electrical power of 80 W, a diameter of 25 mm, a focal length of 20 mm, and a focal point size of $1 \times 1 \times 5 \text{ mm}^3$. Under MR guidance, the HIFU focal point was positioned at the center of the tissue sample. Two 30-second HIFU sonication trials were performed prior to the main HIFU experiment to verify the position of the HIFU focal point. Two fiber-optic probes (Micronor Sensors, Inc., Ventura, CA, USA) were inserted into the tissue – one placed approximately 3 mm and the other 30 mm from the HIFU focal point – to monitor internal temperature and serve as reference temperature measurements. The positions of the temperature probes were verified using 3D Cartesian T1-weighted gradient-echo images (FOV = $278 \times 191 \times 66 \text{ mm}^3$, resolution = $1.08 \times 1.08 \times 1.1 \text{ mm}^3$, TE/TR = 2.58/4.19 ms). HIFU sonication

was triggered at 30 seconds after the start of continuous MR acquisition and continued for 180 seconds at a constant electric power of 30 W.

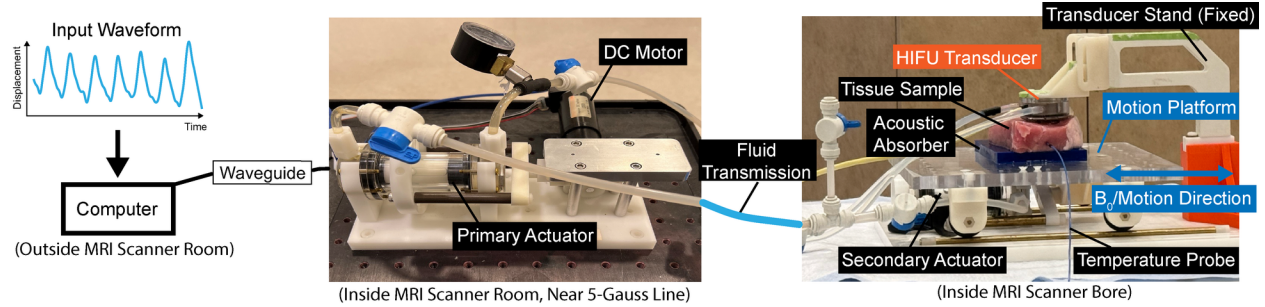


Figure 3-3. The setup of our ex vivo tissue motion phantom high-intensity focused ultrasound (HIFU) experiment. A custom MR-compatible motion platform with a pair of hydrostatic actuators is used to emulate 1D respiratory motion along the B_0 direction. A motion waveform pre-recorded from a healthy human subject with a peak-to-peak amplitude of 16 mm is used as the input. MRI-guided HIFU ablation is performed on a tissue specimen using an 8-element transducer. The transducer position is fixed to the patient table while the tissue sample undergoes motion. Two fiber optic temperature probes are inserted into the tissue sample for temperature validation. The four-channel flexible coil array (not shown) is placed on the HIFU transducer stand and does not move with the motion phantom.

Motion tracking accuracy was assessed by comparing the iNAV signals with the input motion waveform using the Pearson correlation coefficient (CC). Temperature mapping accuracy was evaluated by calculating the temporal mean absolute error (tMAE) between the PRF-based temperature measurements and the temperature probe readings. 3×3 ROIs surrounding the tips of the two temperature probes were selected and averaged for PRF calculation, and their S/I positions were dynamically updated using iNAV processing in **Equation 3-2**. Bland-Altman analysis and root mean square error (RMSE) were used to assess the agreement between the PRF temperature measurements and probe readings during HIFU heating. Single baseline (SB) PRF thermometry was implemented using a single baseline phase image near the EOE position from the baseline library and compared with iNAV-MB PRF.

3.2.6 In Vivo Non-Heating Swine Experiment

The animal study was approved by the UCLA animal research committee (ARC 2022-074). Two Oncopig subjects with induced liver tumors¹⁰⁷ (Duroc, male) and one healthy swine subject (Yorkshire, male), each weighing 30-40 kg, were used to evaluate the framework under non-heating conditions and controlled respiratory cycles set at 5 seconds/breath. The swine subjects were sedated with intramuscular tiletamine hydrochloride–zolazepam hydrochloride (7 mg/kg, Telazol; Fort Dodge Laboratories, Fort Dodge, Iowa).

iNAV motion tracking was compared with the reference periodic signal pattern from mechanical ventilation. To evaluate temperature stability in a motion-compensated, non-heated region while avoiding potential motion artifacts from the tissue boundary, a 3D rectangular liver ROI with dimensions of $25 \times 25 \times 7$ voxels was manually selected within the homogeneous region in the mid liver using the magnitude image at the EOE position and dynamically updated using iNAV processing in **Equation 3-2**. The tMAE and temporal standard deviation (tSD) of the PRF-based temperature were calculated on a voxel-by-voxel basis within the 3D ROI, relative to the expected temperature change of 0 °C. The resulting voxel-wise tMAE and tSD values were then averaged spatially across the ROI for each thermometry method. Both the ex vivo and in vivo experiments were performed on a 3 T MRI scanner (MAGNETOM Prisma, Siemens Healthineers, Erlangen, Germany) using a spine coil array and a 4-channel flexible coil array. The sequence and reconstruction parameters are listed in **Table 3-1**.

Table 3-1. Imaging parameters for the 3D stack-of-radial MRI thermometry technique used in ex vivo motion phantom high-intensity focused ultrasound (HIFU) ablation experiments and in non-heating in vivo swine experiments. All experiments were performed at 3T.

	Ex vivo Motion Phantom HIFU Ablation	In vivo Swine Model
FOV (mm ³)	230×230×72	300×300×72
Resolution (mm ³)	1.79×1.79×3	1.56×1.56×3
Scan Orientation	Axial	Axial
Flip Angle (°)	9	9
TR (ms)	5.13	5.08
TE (ms) *	1.31 / 2.57 / 3.83	1.31 / 2.57 / 3.83
Bandwidth (Hz/px)	1130	1150
Total Radial Angles	3500	1500
Total Scan Time (min:sec)	7:10	3:02
Reference Respiration Period (sec/breath)	~5.4	5
No. Radial Angles in Center/ in Total k-space Region of KWIC Filter	8 / 89	8 / 89
Effective Temporal Resolution / Temporal Footprint of Dynamic PRF Maps using KWIC Reconstruction (sec/volume)	0.98 / 10.96	0.98 / 10.85
No. Radial Angles in Each / in Total Temporal Frame(s) of GRASP Reconstruction Window	8 / 88	8 / 88
Effective Temporal Resolution / Temporal Footprint of Dynamic PRF Maps using GRASP Reconstruction (sec/volume)	0.98 / 10.83	0.98 / 10.73
Number of Baseline Images	20	30

*The magnitude images from the three TEs were combined to improve SNR for image-based motion navigation. The phase images from the last TE were used for temperature map calculation.

3.3 Results

3.3.1 Ex vivo Motion Phantom HIFU Ablation Experiment

Figure 3-4 compares the extracted iNAV motion curves with the reference input waveform over 100 seconds of the ex vivo motion phantom HIFU ablation experiment. The same dataset was used to extract iNAV with two reconstruction methods, KWIC and GRASP, each with varying temporal footprints. **Figure 3-4 (A-D)** shows the iNAV results using KWIC reconstruction by grouping 55 (KWIC-55), 89 (KWIC-89), 144 (KWIC-144), and 233 (KWIC-233) radial angles for each KWIC reconstruction window. **Figure 3-4 (E-H)** shows the iNAV results using GRASP reconstruction by grouping 56 (GRASP-56), 88 (GRASP-88), 144 (GRASP-144), and 232 (GRASP-232) radial angles within each GRASP reconstruction window, selected to match the choice of KWIC temporal footprints for direct comparison. Both KWIC and GRASP reconstruction used the same effective temporal resolution of 0.98 seconds/volume (corresponds to 8 radial angles to fill the central k-space region). The iNAV curve calculates the relative motion displacement compared to a frame at the EOE position. The CC values between the iNAV motion curves and the input waveform are labeled in each subplot.

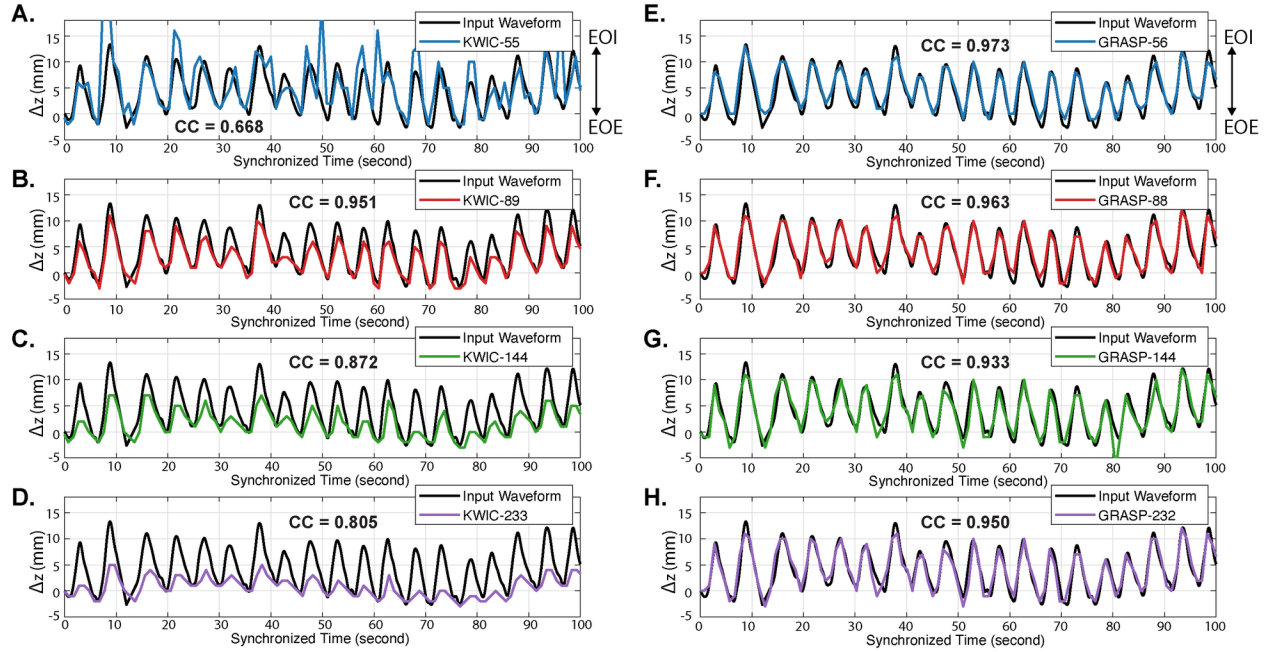


Figure 3-4. Image-navigated (iNAV) motion tracking results during the ex vivo motion phantom experiment compared to the reference input waveform. **(A-D)** iNAV motion tracking result using KWIC reconstruction with different number of radial angles that corresponds to KWIC temporal footprint (e.g., KWIC-89), and **(E-H)** iNAV results using GRASP reconstruction with different number of radial angles that corresponds to GRASP temporal footprint (e.g., GRASP-88). The number of radial angles that correspond to the effective temporal resolution was set to 8 for all cases. KWIC reconstruction needs to strike a balance between inaccurate motion tracking due to undersampling artifacts (i.e., in KWIC-55) and a reduced range of motion (i.e., in KWIC-233), likely due to temporal blurring associated with the use of a larger temporal footprint for the KWIC filter. On the other hand, GRASP reconstruction preserved temporal sharpness with different choices of temporal footprint. Pearson correlation coefficient (CC) with respect to the input waveform is labeled in each of the plots.

Among KWIC reconstruction results, KWIC-89 provided the best tradeoff between motion fidelity and preserved motion range, achieving a $CC = 0.951$. In contrast, all GRASP reconstructions demonstrated consistently high motion tracking accuracy, with CC values exceeding 0.93. GRASP-56 yielded the highest correlation ($CC = 0.973$), while GRASP-88 achieved a comparable performance ($CC = 0.963$) and offered a temporal resolution most similar

to KWIC-89. Based on these findings, KWIC-89 and GRASP-88 were selected for temperature mapping and subsequent in vivo analysis.

Figure 3-5 presents the PRF temperature mapping results during HIFU ablation. The multi-baseline library consisting of $M=6$ motion states was constructed from 20 dynamic images before HIFU heating. The proposed iNAV-MB PRF method effectively reduced motion-induced temperature errors compared to the SB PRF method at both the EOE and end-of-inspiration (EOI) positions. Compared to KWIC reconstruction, the temperature maps from GRASP reconstruction exhibited sharper definition of the HIFU focal point and had fewer residual errors in the non-heating regions.

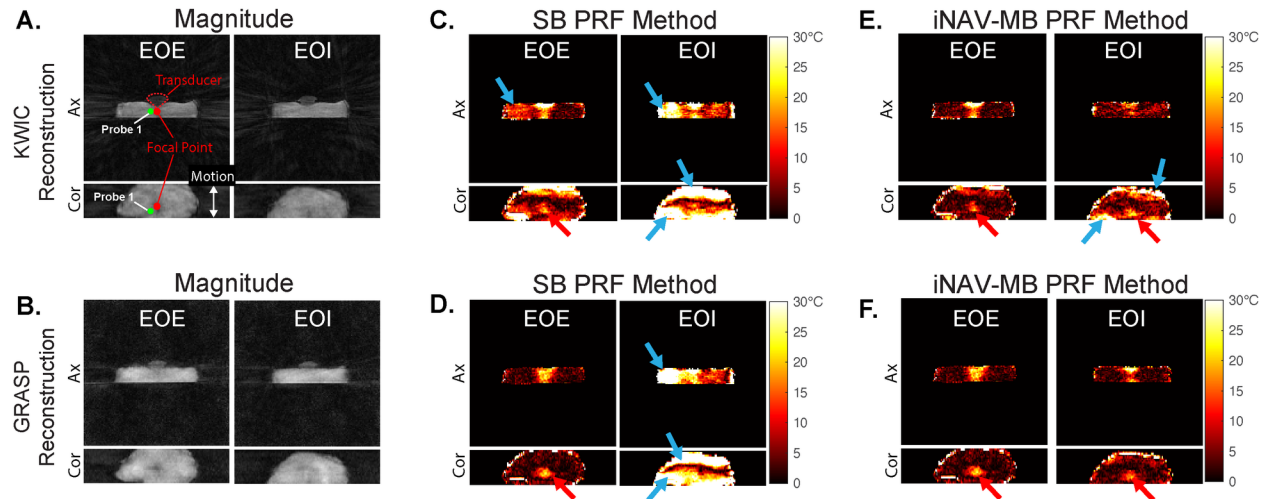


Figure 3-5. 3D PRF absolute temperature change maps of the ex vivo motion phantom HIFU experiment using KWIC and GRASP reconstructions. **(A-B)** Reconstructed magnitude images from two frames corresponding to the end-of-expiration (EOE) and end-of-inspiration (EOI) positions before the conclusion of HIFU ablation. **(C-D)** PRF temperature maps using a single baseline (SB) phase image. **(E-F)** PRF temperature maps using iNAV-MB PRF thermometry consisting of six motion states. The white double-arrows indicate the motion direction (along S/I direction). The green circle indicates the ROI placed at the approximate location of temperature probe 1 near the HIFU focal point. The proposed iNAV-MB PRF method effectively suppressed motion-induced temperature errors in SB PRF at EOI positions. Compared to KWIC reconstruction, the temperature maps from GRASP reconstruction yielded a sharper HIFU focal point at both EOE and EOI positions (red arrows) and less residual temperature errors in non-

heating regions (blue arrow). The backgrounds in PRF maps are masked out using their corresponding magnitude images.

The current version of our 3D stack-of-radial thermometry research sequence supports a maximum of 3500 acquired radial angles and therefore we focused on the HIFU heating and the initial cooldown period for PRF thermometry evaluation. **Figure 3-6** shows the PRF temperature change evolution and temperature probe readings over a 350-second time span. Compared to the temperature probe readings, KWIC reconstruction achieved a tMAE of 1.80 °C in the heating region, whereas GRASP reconstruction achieved a tMAE of 1.44 °C. In non-heating regions, the tMAE was 1.52 °C and 0.73 °C for KWIC and GRASP reconstructions, respectively. Note that the brief temperature “plateau” observed immediately after HIFU sonication in **Figure 3-6C and 3-6E** can be attributed to heat diffusion from the HIFU focal point, as both the PRF ROI and temperature probe were positioned adjacent to (but not directly at) the HIFU focus. For reference, the extended temperature evolution recorded by temperature probes is shown in **Figure 3-7**. **Figure 3-8** presents the Bland-Altman plots, where the mean differences between PRF thermometry and temperature probe readings during HIFU heating were -0.47 °C and 0.39 °C for the KWIC + iNAV-MB and GRASP + iNAV-MB methods, with corresponding RMSE values of 1.67 °C and 1.70 °C, respectively.

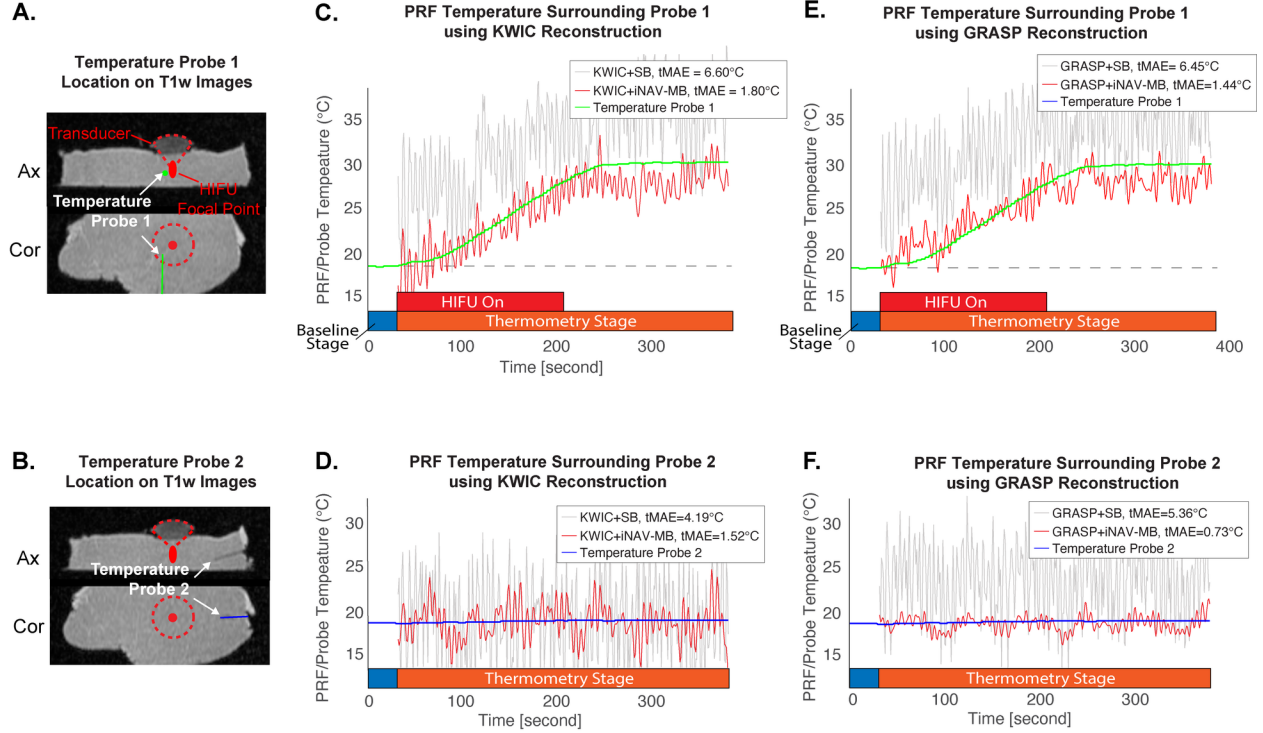


Figure 3-6. Results of the ex vivo motion phantom HIFU ablation experiment. **(A-B)** Locations of two temperature probes on T1-weighted (T1w) images. Probe one was placed approximately 3 mm away from the HIFU focal point, while probe two was placed in a non-heating region approximately 30 mm away from the HIFU focal point. The HIFU focal point is labeled with red circles. **(C-F)** Temperature evolution from 3x3 ROIs extracted from the PRF temperature maps during and after the 180-second HIFU ablation. The ROI locations were dynamically updated using iNAV processing in **Equation 3-2**. The temporal mean absolute errors (tMAE) using the iNAV-MB PRF method relative to the temperature probe readings demonstrated a marked improvement in temperature accuracy compared to the SB PRF method.

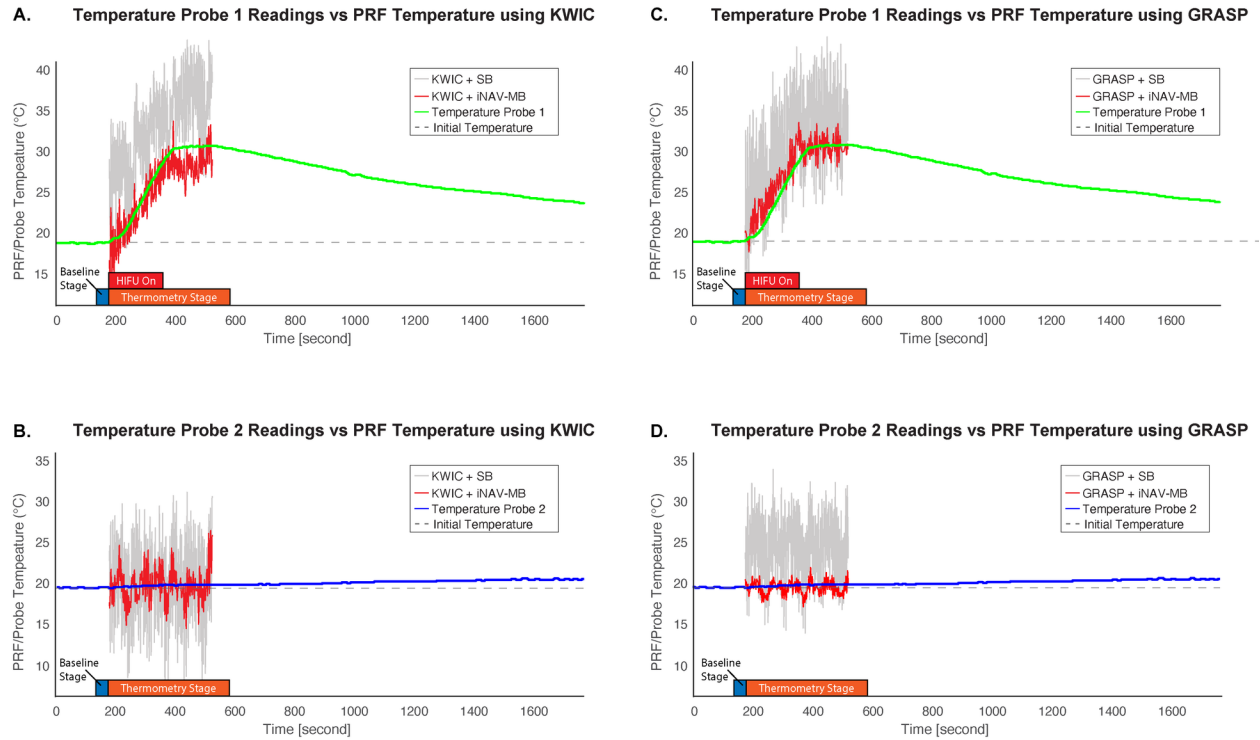


Figure 3-7. Temperature probe readings during the full ex vivo motion phantom experiment, including an extended cooldown period. The probe locations are shown in **Figures 3-6A** and **3-6B**. PRF temperature measurements during the thermometry stage are plotted for reference.

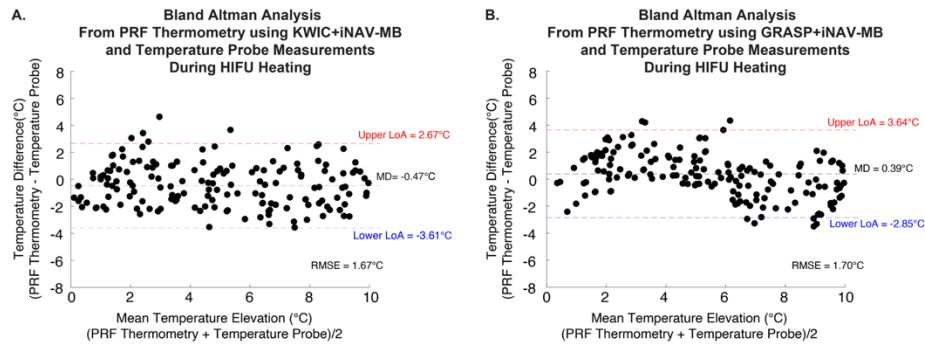


Figure 3-8. Bland-Altman plots comparing PRF thermometry measurements using **(A)** KWIC+iNAV-MB and **(B)** GRASP + iNAV-MB at ROI 1 near the HIFU focal point (see **Figure 3-6A**) with respect to reference temperature probe readings. The mean difference (MD) and 95% limits of agreement (LoA) are labeled in the plots. In addition, root mean square error (RMSE) values are reported.

3.3.2 In vivo Non-Heating Swine Experiments

Figure 3-9 shows the extracted iNAV motion curves from a swine subject under controlled ventilation. The same dataset was reconstructed using KWIC-89 and GRASP-88, respectively, to generate the iNAV signals. Both methods captured the periodic breathing pattern, consistent with the expected 5-second respiratory cycle. GRASP reconstruction resolved more distinct motion positions, with clearer transitions between the EOI and EOE positions, whereas KWIC tended to average between these positions, likely due to temporal smoothing. GRASP also exhibited a slightly larger motion range in the S/I direction, although this difference with KWIC was less pronounced than in the ex vivo experiment.

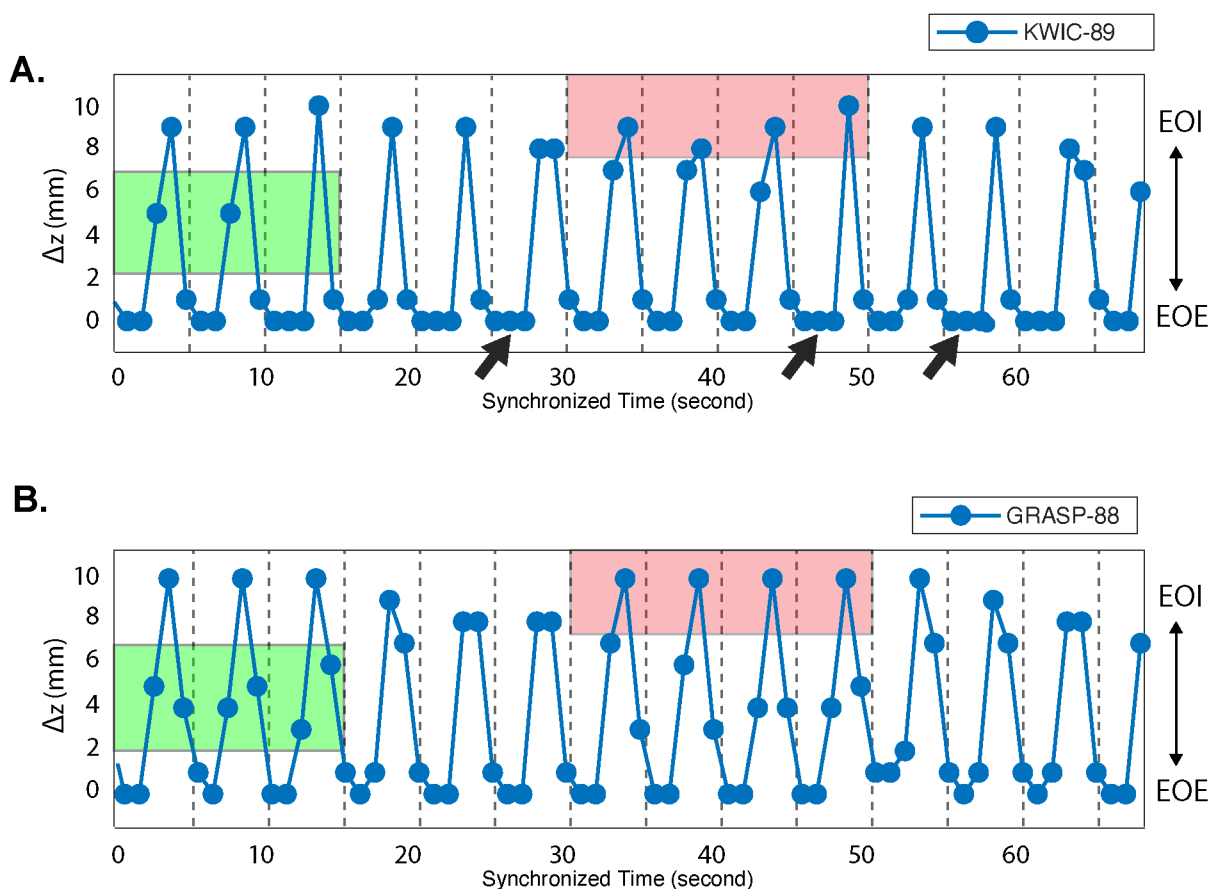


Figure 3-9. iNAV motion tracking results from an in vivo swine subject under controlled ventilation with (A) KWIC reconstruction with 89 radial angles within each reconstruction

window and **(B)** GRASP reconstruction with 88 radial angles within each reconstruction window. Gray vertical lines indicate the reference respiratory period set at 5 seconds/breath. GRASP reconstruction resolved more distinct motion positions (green shaded region) and a larger range of motion (red shaded region) compared to KWIC reconstruction. The iNAV results from KWIC exhibited “plateaus” at end-of-expiration (black arrows), likely due to the motion averaging effects.

Figure 3-10 shows the temperature mapping results using a baseline library consisting of 30 dynamic images under non-heating conditions from the same swine subject in **Figure 3-9**. The proposed iNAV-MB PRF method effectively suppressed motion-induced temperature errors within the liver volume compared to the SB PRF method. Compared to the PRF maps from KWIC reconstruction, those from GRASP reconstruction exhibited less temperature variation in the liver, where no heating was expected.

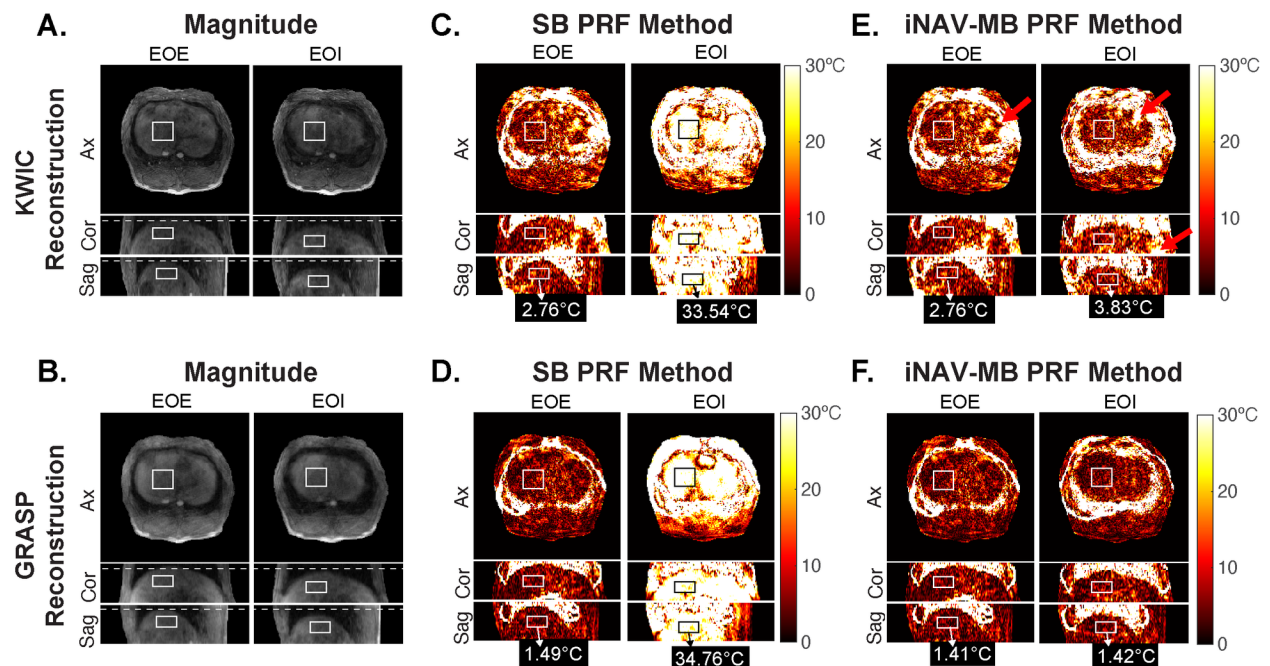


Figure 3-10. 3D PRF absolute temperature change maps from a representative swine subject (same as in **Figure 3-9**) during the in vivo non-heating experiment. **(A-B)** Reconstructed magnitude images from two selected frames corresponding to the EOE and EOI positions using KWIC and GRASP reconstruction. **(C-D)** PRF temperature maps using a single baseline (SB) phase image from EOE position and **(E-F)** using iNAV-MB PRF methods with six motion states.

Residual temperature errors are present in KWIC reconstruction results (red arrows). The white and black rectangular ROIs indicate a 3D liver region-of-interest with size $25 \times 25 \times 7$ voxels. The spatially averaged mean absolute temperature errors in this 3D volume at each frame are reported at the bottom of the temperature maps, relative to the expected temperature change of 0°C (no heating). The positions of the 3D ROIs were dynamically updated continuously using iNAV processing, and their locations were dynamically updated using **Equation 3-2**. White dashed lines indicate reference liver positions.

Across all three swine subjects, the tSD for KWIC reconstruction decreased markedly from $7.13\text{--}8.19^\circ\text{C}$ (median of 8.03°C) with the SB PRF method to $3.74\text{--}3.86^\circ\text{C}$ (median of 3.85°C) with the iNAV-MB PRF method. Similarly, the tSD for GRASP reconstruction was substantially reduced from $4.77\text{--}7.82^\circ\text{C}$ (median of 7.23°C) with the SB PRF method to $1.76\text{--}2.43^\circ\text{C}$ (median of 2.37°C) with the iNAV-MB PRF method. Key results from the in vivo non-heating swine experiments are summarized in **Table 3-2**.

Table 3-2. Summary of the temperature mapping results from the in vivo non-heating swine experiments. The temporal mean absolute error (tMAE) and temporal standard deviation (tSD) from the dynamically updated 3D ROIs (as shown in **Figure 3-10**) were computed on a voxel-by-voxel basis, and the spatial averages across the ROI were reported for each thermometry method. Bold font indicates the temperature mapping method with the best performance. KWIC: k-space weighted image contrast; GRASP: golden-angle radial sparse parallel MRI; PRF: proton resonance frequency shift; SB: single baseline PRF method; iNAV-MB: image-navigated multi-baseline PRF method.

	Swine Subject 1		Swine Subject 2		Swine Subject 3	
	tMAE($^\circ\text{C}$)	tSD($^\circ\text{C}$)	tMAE($^\circ\text{C}$)	tSD($^\circ\text{C}$)	tMAE($^\circ\text{C}$)	tSD($^\circ\text{C}$)
KWIC + SB	28.99	8.03	9.72	8.19	13.95	7.13
GRASP + SB	28.31	7.82	9.33	7.23	13.05	4.77
KWIC + iNAV-MB	3.33	3.74	3.45	3.86	3.25	3.85
GRASP + iNAV-MB	2.50	2.37	2.09	2.43	1.48	1.76

3.4 Discussion

This work developed a stack-of-radial MRI-based approach for rapid volumetric thermometry in moving tissues, such as liver, achieving continuous 3D temperature mapping with 24 axial slices (3-mm thickness), in-plane resolution of 1.6×1.6 to 1.8×1.8 mm², and an effective temporal resolution of 0.98 seconds/volume. To address the motion-induced baseline mismatch, we proposed an image-navigated multi-baseline technique, or iNAV-MB, to directly estimate and correct motion during multi-baseline PRF thermometry. Two radial MRI reconstruction methods, KWIC and GRASP, were implemented and adapted for dynamic PRF thermometry using a sliding window approach. We compared the combination of KWIC and iNAV-MB to the combination of GRASP and iNAV-MB and evaluated their performance in measuring temperature changes during respiratory motion. The performance of these two approaches was validated through an ex vivo tissue motion phantom HIFU ablation experiment and achieved a temperature tMAE of < 1.5 °C during HIFU ablation compared to the temperature probe readings. For in vivo non-heating swine experiments, we achieved temperature mapping precision in terms of tSD of 3.74-3.86 °C and 1.76-2.43 °C for the combination of KWIC + iNAV-MB and GRASP + iNAV-MB, respectively, within motion-compensated 3D liver ROIs across three swine subjects.

3.4.1 Stack-of-Radial MRI-Based Volumetric Thermometry

Stack-of-radial MRI offers an advantageous solution for volumetric PRF thermometry in moving tissues, due to its inherent robustness to motion and flexibility in balancing spatiotemporal resolution. While prior studies have demonstrated the feasibility of stack-of-radial-based PRF

thermometry in largely static organs^{40,41} (i.e., brain, breast, prostate), our work successfully extended this technique to abdominal organs, such as the liver, in the presence of continuous respiratory motion. GRASP, on the other hand, had not been previously investigated for PRF temperature mapping.

In contrast to EPI-based thermometry methods^{43,50,86,87,89,90,108}, which are typically constrained to 2D acquisitions or limited slice coverage, stack-of-radial acquisitions enable true 3D temperature monitoring. A recent EPI-based study extended slice coverage using simultaneous multi-slice acquisition with multiband acceleration, achieving 12-slice coverage at 700 ms per volume in a moving phantom¹⁰⁹. However, higher multiband factors degraded imaging quality due to aliasing. Our stack-of-radial approach overcame this limitation by supporting higher undersampling factors – up to 25-fold ex vivo and 38-fold in vivo based on Nyquist criteria – while maintaining image fidelity, as demonstrated by clear delineation of tissue boundaries and ablation zones (**Figures 3-5 and 3-10**). This framework enabled dynamic 3D temperature mapping across 24 axial slices and around 1 second effective temporal resolution per volume, a substantial advance in volumetric coverage for dynamic PRF thermometry in moving tissues. While the echo time (TE=3.83ms) we used for thermometry was shorter than those typically used for maximizing temperature-to-noise ratio, it was chosen to prioritize temporal resolution and volumetric coverage, both critical for monitoring thermal therapies in moving abdominal organs. Further improvements in volumetric coverage or temporal resolution may be possible by incorporating more efficient sampling strategies such as stack-of-radial with k_z undersampling¹¹⁰ or stack-of-radial EPI hybrid techniques¹¹¹.

Our swine study was designed to closely mimic the clinical setup, including coil placement, use of general anesthesia, and respiratory cycle duration¹¹². Therefore, a similar level of temperature mapping performance is expected when translating to human subjects. However, recalibration of KWIC and GRASP reconstruction parameters will be necessary to accommodate differences in respiratory patterns, body size, and tissue composition.

3.4.2 Advantages of iNAV-MB

We developed an image-navigated multi-baseline PRF thermometry method that leveraged the reconstructed magnitude images to guide multi-baseline temperature mapping. While previous motion navigation methods for PRF thermometry often relied on separate 1D or 2D navigator echo acquisitions^{104,113}, our iNAV approach extracted motion directly from the magnitude image data itself, enabling motion self-navigation without the need for additional acquisition modules. In our iNAV approach, motion was estimated by comparing dynamic magnitude images to a baseline frame using a region containing distinct features to achieve frame-to-frame tissue displacement tracking. A multi-echo acquisition was used to improve magnitude image SNR and enhance tissue boundary contrast for robust navigation. The extracted iNAV motion information was used throughout the multi-baseline PRF thermometry pipeline for baseline image sorting, dynamic image matching, and target ROI tracking. Compared to a previous trajectory-based navigator-free method proposed by Svedin et al.⁴¹, which relied on pseudo-golden-angle matching of k-space data for implicit motion correction, our approach directly estimated motion displacement to enable explicit, active motion tracking, which is a requirement for applications such as HIFU beam steering¹¹⁴ or robotic-assisted interventions¹¹⁵.

Another major advantage of our iNAV-MB method is that it enables respiratory motion tracking in the dominant S/I direction without requiring acquisition in specific planes, whereas previous multi-baseline techniques were limited to sagittal or coronal acquisitions^{43,50,108}. This flexibility is enabled by the high effective temporal resolution and volumetric coverage of the stack-of-radial sequence. As validated in the motion phantom experiment (**Figure 3-4**), iNAV-MB achieved high motion tracking accuracy under a variable breathing pattern. This enabled continuous temperature mapping across all motion states, with markedly improved temperature stability and reduced errors compared to single-baseline PRF. Nevertheless, the single-baseline approach using GRASP demonstrated good temperature stability when the motion position matched the baseline phase image (**Figures 3-5D and 3-10D**). Therefore, a motion-gated approach, such as using a data acceptance window at EOE, could be a practical alternative when monitoring a specific motion state is preferred, albeit at the cost of skipping time frames at other motion states. Although this study focused on tracking motion in the S/I direction, the proposed framework can be extended to incorporate anterior-posterior and left-right motion components in future implementations to enable comprehensive 3D motion tracking.

3.4.3 KWIC vs. GRASP Reconstruction

KWIC and GRASP reconstruction techniques employ different strategies in how they fill in k-space and handle temporal information, leading to differences in motion tracking fidelity and PRF temperature mapping accuracy. KWIC reconstruction uses a k-space filtering strategy where the low-frequency central k-space region, which is critical for overall image contrast and contains slow-changing spatial temperature information, is updated frequently using data from a narrow temporal window. Meanwhile, the high-frequency peripheral k-space regions, which

capture finer structural details and rapidly changing spatial features, are filled with a broader set of spokes collected over a longer period. This filtering strategy helps suppress undersampling artifacts (**Figure 3-5A and 3-10A**), capture overall motion periodicity (**Figure 3-4 A-D**), and measure the temperature changes (**Figure 3-6C**). We implemented a backward-looking KWIC filter configuration to ensure a timely update of the central k-space region. However, KWIC filtering will introduce averaging effects due to a mixing of motion and temperature information in the peripheral k-space regions, especially if the temporal footprint is not carefully optimized. As shown in **Figure 3-4A-D**, broader temporal footprints led to more severe averaging effects with reduced apparent tissue displacement, while a shorter temporal footprint improved motion fidelity but increased the risk of errors resulting from undersampling artifacts. These effects can also degrade temperature accuracy, especially when thermal gradients evolve quickly in the tissues. To balance these effects, we identified an optimal configuration for our experimental data using KWIC with 8 radial angles in the center of k-space and 89 radial angles in the full reconstruction window and achieved a motion tracking CC of 0.951 relative to the input waveform and a temperature accuracy of 1.80°C compared to reference probe data. Such motion averaging effects were less pronounced during in vivo experiments with mechanical ventilation, likely due to higher SNR and more regular breathing patterns compared to the phantom study. These results suggest that while KWIC offers fast, real-time compatible reconstructions, their use should be cautioned in scenarios requiring more precise motion and temperature monitoring where averaging effects may lead to underestimation of temperature rise or tissue displacement amplitude.

In contrast, GRASP uses a compressed sensing reconstruction framework that balances data consistency and temporal sparsity along the temporal direction. The golden-angle-ordered radial sampling trajectory provides flexible k-t sampling to support arbitrary temporal grouping as well as incoherent undersampling artifacts. GRASP jointly reconstructs several temporal image frames within a single reconstruction window without explicit data sharing between the frames, maintaining data fidelity and temporal stability in low- and high-frequency k-space regions. This approach avoids the data mixing effects inherent to KWIC and enables reconstruction of the full-resolution k-space data, making it suitable for both motion tracking and dynamic temperature mapping, even at high undersampling rates. In this work, GRASP reconstruction demonstrated excellent motion tracking accuracy across a range of temporal footprints (**Figure 3-4E-H**), highlighting its robustness to averaging effects that were associated with KWIC. In the in vivo experiments, GRASP also resolved more distinct motion positions and preserved a wider motion range compared to KWIC, as shown in **Figure 3-9**, consistent with the trends observed in the ex vivo experiments. Moreover, GRASP achieved higher temperature accuracy during the ex vivo experiment in both heating and non-heating regions, with a tMAE of 1.44 °C and 0.73 °C, respectively. In contrast, KWIC yielded higher tMAE values of 1.80 °C and 1.52 °C in the same regions. In the in vivo experiments, GRASP demonstrated improved temperature mapping performance in both tMAE and tSD compared to KWIC. This higher precision in temperature mapping could enable more accurate cumulative thermal dose estimation, which is critical for assessing treatment outcomes in thermal ablation. However, GRASP's main drawback remains the intensive computational cost. Our implementation required approximately 62.5 seconds to reconstruct a single 2D slice from one reconstruction window, limiting its use for real-time applications. In addition, GRASP's temporal update step size equals the full span of the GRASP

reconstruction window (as shown in **Figure 3-1F**), resulting in the generation of several time frames at once but at a slower update step size of 10 seconds using the parameters listed in **Table 3-2**. In contrast, KWIC reconstruction does not require an iterative approach and enables more frequent updates, as its temporal update step size depends only on the radial spokes in the central k-space region (as shown in **Figure 3-1E**). These make KWIC more suitable for scenarios where immediate temperature feedback is required. Reducing the GRASP temporal footprint (e.g., using GRASP-56 instead of GRASP-88) may slightly shorten reconstruction time by lowering the number of k-space samples; however, the overall latency remains primarily dominated by the iterative optimization process. Future studies should investigate optimizing GRASP parameters, such as using shorter temporal footprints and fewer spokes to enable more frequent updates without compromising temperature mapping performance. Accelerated reconstruction techniques, including GPU-based implementations¹¹⁶ or deep learning approaches^{117,118}, may enhance the feasibility of 3D non-Cartesian stack-of-radial MRI for real-time volumetric temperature monitoring.

3.4.4 Limitations and Future Directions

There are limitations to this study. First, while the current implementation of KWIC and GRASP reconstruction utilized GPU-based non-uniform Fast Fourier Transform¹¹⁹ to accelerate radial MRI reconstruction, the processing was performed offline in a retrospective manner and is not yet ready for real-time temperature monitoring. Further improvements are needed in optimized software implementation¹²⁰ and integration with online reconstruction frameworks, such as using Gadgetron^{121,122}. Second, the current iNAV-MB method measures rigid body motion along the S/I direction. While this strategy was effective for pre-recorded breathing patterns from healthy

human subjects and controlled ventilation in swine, more complex motion patterns, such as non-rigid deformation or irregular breathing, may require more comprehensive motion-compensation techniques, such as non-rigid motion estimation^{123,124} or incorporation of anterior-posterior and left-right motion components¹²⁵. Third, this study validated the proposed thermometry framework through a single ex vivo HIFU ablation experiment with a single respiratory waveform. Future studies should evaluate performance under a wider range of motion patterns, ablation protocols, as well as in vivo ablation to better establish generalizability for clinical translation.

3.5 Conclusion

We developed and validated a volumetric MR thermometry framework for moving tissues, based on a golden-angle-ordered stack-of-radial 3D MRI acquisition combined with dynamic radial reconstruction using KWIC and GRASP, image-based motion tracking, and multi-baseline PRF thermometry. This approach enables high spatiotemporal resolution and motion-compensated 3D temperature monitoring in moving tissues, offering marked improvement in volumetric coverage over conventional methods. The proposed volumetric thermometry framework can be a potential solution for improving the accuracy and robustness of MR-guided thermal ablations in moving organs.

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navigated multi-baseline proton resonance frequency shift method. *Magnetic Resonance in Medicine*. 2026;95(2):803–819. doi:10.1002/mrm.70074.

CHAPTER 4 ACTIVE ELECTROMAGNETIC INTERFERENCE SUPPRESSION FOR MRI AND PROTON RESONANCE FREQUENCY SHIFT THERMOMETRY DURING MRI-GUIDED MICROWAVE ABLATION

4.1 Introduction

Microwave ablation (MWA) is a common thermal ablation technique for treating non-resectable primary and metastatic liver tumors⁷⁵. Compared to the more established radiofrequency (RF) ablation technology, MWA offers several key advantages, such as faster heating¹²⁶, the ability to achieve larger coagulative volumes with multiple applicators¹²⁷, and decreased susceptibility to heat-sink effects from nearby blood vessels^{128,129}. Due to these benefits, MWA has become the preferred ablation modality for treating very-early-stage and early-stage hepatocellular carcinoma (HCC), as well as other liver malignancies for non-surgical patients^{75,130}.

Effective thermal ablation must balance achieving clear ablation margins (5-10 mm) around the tumor while minimizing inadvertent damage to nearby structures¹¹. Reliable intraprocedural temperature monitoring is therefore critical to provide real-time feedback on ablation zone formation, ensuring adequate margins to achieve complete treatment while maintaining safety. Conventional image-guided approaches, such as computed tomography (CT)⁷⁹ or ultrasound (US)⁷⁸, track microbubble formation, a surrogate marker for vaporization that does not reliably represent the extent of ablation zone progression. Magnetic resonance imaging (MRI), in contrast, provides excellent soft tissue contrast and flexible scan orientations, offering unique advantages for treating lesions poorly visualized on CT/US^{30,131}. In addition, proton resonance frequency (PRF) shift-based MR thermometry enables non-invasive temperature monitoring,

providing real-time temperature mapping and thermal dose estimation⁸⁰. The feasibility of MR thermometry for MRI-guided MWA has been demonstrated in treating prostate⁴⁷ and liver cancer^{51,112,132}.

Despite these promising advancements, the clinical adoption of MRI-guided MWA remains limited. A major obstacle is the electromagnetic interference (EMI) emitted from the MWA systems, which contaminates MRI k-space data and leads to noise-like artifacts in the reconstructed images^{47,51,53,132,133}. The primary source of EMI comes from imperfect shielding of the microwave generator and system components during active operation inside the RF-shielded MRI scanner room. Additionally, even when the generator is placed outside the scanner room, EMI and ambient RF noise may still propagate into the scanner room via the coaxial cable^{47,51,53,133}. As a result, EMI-induced MR image degradation severely compromises intraprocedural monitoring by obscuring the depiction of tissue structures and delineation of ablation zone boundary, and leads to errors in PRF temperature measurements. To date, most EMI-suppression strategies for MRI-guided MWA have relied on either hardware modifications (e.g., adding physical shielding or filters^{51,53,132,134}) or intermittent ablation strategies (pausing heating during image acquisition^{47,135}). These approaches, however, require specialized equipment or equipment modifications, disrupt the ablation protocols, or are impractical for routine clinical workflows.

Software-based EMI suppression techniques offer greater flexibility than hardware-based and workflow modification-based approaches. Because EMI presents as a structured pattern in k-space, it can be identified and suppressed during image reconstruction and post-processing,

thereby avoiding system modification or interruptions to the clinical ablation workflow. For instance, a prior study used a threshold-based approach to identify contaminated k-space data and replaced it with previously acquired non-contaminated data¹³³. However, this data substitution technique resulted in residual EMI-related artifacts. Alternatively, model-based active EMI suppression (AES) techniques directly predict and subtract EMI from the tissue MR signals^{136,137}. The AES approach is uniquely advantageous because it can be integrated into the MRI reconstruction pipeline without disrupting the ablation workflow or modifying the imaging sequence. However, previous AES implementations focused on characterizing ambient EMI in unshielded point-of-care MRI settings, and their effectiveness against MWA-induced EMI has not been investigated. Moreover, since previous AES methods were optimized for single-receiver-coil ultra-low-field MRI systems with dedicated EMI sensors, developing AES for clinical whole-body MRI systems with phased array multi-channel receiver coils requires further research.

The goal of this study was to develop and evaluate a software-based AES framework to suppress ablation-device-related EMI and enable robust MRI and MR thermometry during MRI-guided MWA on whole-body multi-channel MRI systems. The proposed AES framework leverages an additional set of standard receiver coils for EMI detection and characterization. The unwanted EMI was then modeled and suppressed from the acquired imaging k-space data on a frame-by-frame basis, without the need for pre-acquired imaging data, equipment modification, or workflow disruption. We evaluated the proposed AES framework through MWA experiments in gel phantoms and in vivo pig models on a 3T MRI system with parallel imaging acceleration.

4.2 Theory

The proposed AES framework utilizes two sets of receiver coils: “primary coils” for standard image acquisition and “auxiliary coils” for EMI characterization. A standard body array coil is positioned at the foot of the patient bed to serve as the auxiliary coils (**Figure 4-1A**). These auxiliary coils are placed outside the imaging volume and remain unloaded (air-filled) to exclusively sense and characterize EMI.

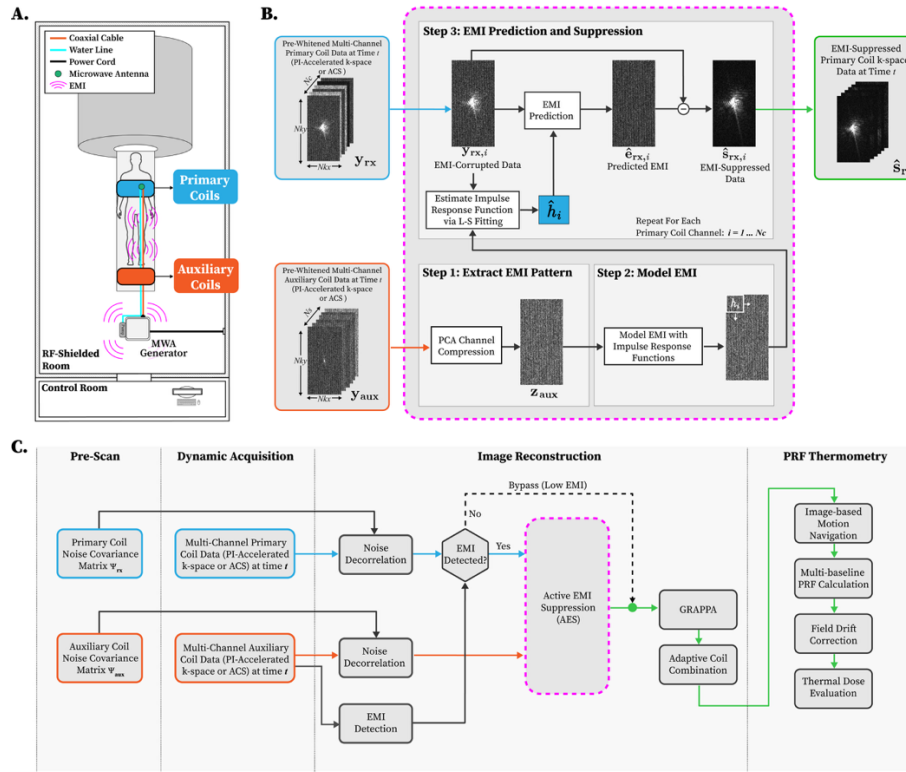


Figure 4-1. Overview of the proposed active EMI suppression (AES) framework for MRI-guided microwave ablation (MWA). **(A)** A schematic drawing of the proposed experimental setup. The MWA system was placed inside the RF-shielded MRI scanner room. In addition to the primary coils (blue) for imaging signal reception, the auxiliary coils (orange) were positioned at the end of the patient bed, outside the imaging field of view, to measure EMI. **(B)** AES algorithm. At each time frame, pre-whitened auxiliary coil data were first compressed using principal component analysis (PCA) to characterize the EMI pattern z_{aux} . The EMI contribution to each primary coil channel i was modeled using a channel-specific impulse response function h_i and solved via least-squares (L-S) fitting. The predicted EMI was then subtracted from the original primary coil k-space data to yield EMI-suppressed data. See the Theory section for mathematical details. **(C)** Parallel imaging accelerated reconstruction and PRF thermometry

pipeline. AES and noise decorrelation were independently applied to both the undersampled imaging k-space data and the autocalibration (ACS) data before GRAPPA reconstruction. A PCA-based detector identified EMI-contaminated frames when the percentage of total variance explained by the first principal component relative to the cumulative variance of all principal components derived from auxiliary coil data (ρ_1) exceeds a threshold of 95%. The reconstruction pipeline with noise decorrelation alone (without AES) served as the baseline for comparison.

4.2.1 Signal Model

Building on the linear convolution framework for active EMI suppression introduced by Srinivas et al.¹³⁶ for single-receiver-coil systems, we extend the formulation to MRI systems with multi-channel receiver arrays. Without loss of generality, the presented theory is shown for the exemplary case of 2D Cartesian-sampled MRI and MR thermometry. The k_x and k_y coordinates are used to index discrete sampling points along the frequency- and phase-encoding directions. We consider a dynamic multi-channel MRI acquisition affected by EMI during MWA at a time point t . The measured k-space data from the primary coils $\mathbf{y}_{\text{rx}}$ are modeled as the superposition of the EMI-free signal component $\mathbf{s}_{\text{rx}}$ and the coupled EMI component $\mathbf{e}_{\text{rx}}$:

$$\mathbf{y}_{\text{rx}}(t) = \mathbf{s}_{\text{rx}}(t) + \mathbf{e}_{\text{rx}}(t) \quad (4-1)$$

where $\mathbf{y}_{\text{rx}}, \mathbf{s}_{\text{rx}}, \mathbf{e}_{\text{rx}} \in \mathbb{C}^{N_{k_x} \times N_{k_y} \times N_c}$, with N_{k_x}, N_{k_y} denoting the number of frequency- and phase-encoding steps, and N_c the number of primary coil channels.

Data acquired from the auxiliary coils at the same time point t are described as:

$$\mathbf{y}_{\text{aux}}(t) = \mathbf{s}_{\text{aux}}(t) + \mathbf{e}_{\text{aux}}(t) \quad (4-2)$$

where $\mathbf{y}_{\text{aux}}, \mathbf{s}_{\text{aux}}, \mathbf{e}_{\text{aux}} \in \mathbb{C}^{N_{k_x} \times N_{k_y} \times N_s}$, and N_s denotes the number of auxiliary coil channels.

Since the auxiliary coils are positioned outside the RF-excited imaging volume, their measured

data are expected to be dominated by EMI, and their sensitivity to the excited spins in the imaging volume is negligible, i.e., $\mathbf{s}_{\text{aux}} \approx 0$ and $\mathbf{y}_{\text{aux}} \approx \mathbf{e}_{\text{aux}}$.

4.2.2 Auxiliary Coil Channel Compression

We assume that the EMI originating from the MWA system is from a limited number of sources and resides in a subspace with dimensions much smaller than the number of auxiliary coil channels. Using the full set of auxiliary channels for subsequent EMI modeling introduces redundant degrees of freedom that can degrade the robustness of the convolution kernel estimation. To address this, we compress the auxiliary coil data along the channel dimension using principal component analysis (PCA), retaining only the dominant components that characterize the EMI subspace.

For each time point, the auxiliary coil data are reshaped into matrix form: $\mathbf{Y}_{\text{aux}}(t) \in \mathbb{C}^{N_s \times N_k}$ (where $N_k = N_{k_x} N_{k_y}$), and decomposed using singular value decomposition:

$$\mathbf{Y}_{\text{aux}}(t) = \mathbf{U}(t)\mathbf{\Sigma}(t)\mathbf{V}(t)^H \quad (4-3)$$

where $\mathbf{U}(t)$ contains the left singular vectors, whose columns correspond to the principal components of the auxiliary channel data, $\mathbf{V}(t)$ contains the right singular vectors, and $\mathbf{\Sigma}(t)$ represents the diagonal matrix of singular values. Since EMI generates highly correlated patterns across channels, the variance is concentrated in the first few principal components. Therefore, we retain the first D principal components whose cumulative variance accounts for a sufficient portion of the total variance (e.g., >95%) and discard the remaining components as noise. This truncated set defines the dominant EMI basis $\mathbf{U}_D(t)$:

$$\mathbf{U}_D(t) = [\mathbf{u}_1(t), \dots, \mathbf{u}_D(t)] \quad (4-4)$$

where $u_j(t)$ is the j -th column of $\mathbf{U}(t)$. We then project the original auxiliary coil data onto this lower-dimensional subspace to extract the characterized EMI pattern $\mathbf{Z}_{\text{aux}}(t) \in \mathbb{C}^{D \times N_k}$ for subsequent EMI modeling:

$$\mathbf{Z}_{\text{aux}}(t) = \mathbf{U}_D(t)^H \mathbf{Y}_{\text{aux}}(t) \quad (4-5)$$

4.2.3 EMI Modeling, Estimation, and Suppression

To model the EMI coupled into each primary coil channel, we account for channel-specific geometry and sensitivity. The EMI component is modeled as the convolution of the PCA-compressed auxiliary data (**Section 4.2.2**) with a channel-specific impulse response function. For the i -th primary coil channel, the signal model is expressed in vectorized form as:

$$\mathbf{y}'_{\text{rx},i} = \mathbf{s}'_{\text{rx},i} + \mathbf{E}\mathbf{h}_i \quad (4-6)$$

where $\mathbf{E}$ is the block-Toeplitz convolution matrix constructed from the characterized EMI pattern $\mathbf{Z}_{\text{aux}}$, and $\mathbf{h}_i$ is the concatenated impulse response vector with kernel size of L_x and L_y . The impulse response is estimated via least-squares:

$$\hat{\mathbf{h}}_i = (\mathbf{E}^H \mathbf{E})^{-1} \mathbf{E}^H \mathbf{y}'_{\text{rx},i} \quad (4-7)$$

and the EMI-suppressed data is obtained by subtraction:

$$\hat{\mathbf{s}}_{\text{rx},i} = \mathbf{y}_{\text{rx},i} - \mathbf{E}\hat{\mathbf{h}}_i \quad (4-8)$$

This estimation and suppression process is performed independently for each primary coil channel at each time frame. The complete AES algorithm is summarized in **Figure 4-1B** and detailed in the next section.

4.2.4 AES Algorithm

Input:

$\mathbf{y}_{\text{rx}}(t)$: multi-channel raw k-space data ($N_{k_x} \times N_{k_y}$) from primary coils at time t (N_c channels)

$\mathbf{y}_{\text{aux}}(t)$: multi-channel raw k-space data from auxiliary coils at time t (N_s channels)

τ : cumulative variance threshold (e.g., 95%) for EMI detection

Output:

$\hat{\mathbf{s}}_{\text{rx}}(t)$: EMI-suppressed primary coil k-space data at time t (N_c channels)

Steps:

1. Auxiliary coil data compression to estimate the EMI pattern:

1a. Reshape auxiliary data $\mathbf{y}_{\text{aux}}(t)$ into 2D matrix $\mathbf{Y}_{\text{aux}}(t)$.

1b. Perform singular value decomposition:

$$\mathbf{Y}_{\text{aux}}(t) = \mathbf{U}(t)\mathbf{\Sigma}(t)\mathbf{V}(t)^H$$

1c. Determine the rank D such that the cumulative variance explained by the first D principal components from $\mathbf{\Sigma}(t)$ exceeds τ .

1d. Extract the characterized EMI pattern $\mathbf{Z}_{\text{aux}}(t)$ by projecting onto the first D columns of $\mathbf{U}(t)$:

$$\mathbf{Z}_{\text{aux}}(t) = \mathbf{U}_D(t)^H \mathbf{Y}_{\text{aux}}(t)$$

2. Model EMI as impulse responses:

2a. Reshape $\mathbf{Z}_{\text{aux}}(t)$ back into k-space: $\mathbf{z}_{\text{aux}}(t)$

2b. Construct a convolution matrix $\mathbf{E}(t)$ from $\mathbf{z}_{\text{aux}}(t)$ to represent the linear impulse response model.

3. Channel-wise EMI prediction and suppression:

For each primary coil channel $i = 1 \dots N_c$:

3a. Vectorize primary coil data as $\mathbf{y}'_{\text{rx},i}(\mathbf{t})$

3b. Estimate channel-specific impulse responses via least-squares fitting.

$$\hat{\mathbf{h}}_i(\mathbf{t}) = \underset{\mathbf{h}_i}{\text{argmin}} \|\mathbf{y}'_{\text{rx},i}(\mathbf{t}) - \mathbf{E}\mathbf{h}_i(\mathbf{t})\|_2^2$$

3c. Predict EMI

$$\hat{\mathbf{e}}_{\text{rx},i}(\mathbf{t}) = \mathbf{E}\hat{\mathbf{h}}_i(\mathbf{t})$$

3d. Subtract EMI and recover EMI-suppressed k-space data.

$$\hat{\mathbf{s}}_{\text{rx},i}(\mathbf{t}) = \mathbf{y}_{\text{rx},i}(\mathbf{t}) - \hat{\mathbf{e}}_{\text{rx},i}(\mathbf{t})$$

4.3 Methods

4.3.1 AES Implementation and Image Reconstruction

All data were reconstructed retrospectively in MATLAB R2023b (MathWorks, Natick, MA).

Primary and auxiliary coil channels were first identified from raw k-space data using a reference frame acquired without EMI. AES was applied using a fixed kernel size of $L_x = 3$ and $L_y = 1$ for imaging k-space data and autocalibration signal (ACS) data (when parallel imaging was performed), where the kernel size was selected to balance EMI modeling capability and computational cost similar to the approach in Srinivas et al.¹³⁶

Although AES dynamically estimates and suppresses EMI, applying it to non-contaminated data risks amplifying the noise and altering the actual signal content. To prevent this, an automated EMI detection module was inserted upstream of the AES module (Figure 4-1C). The detection module leverages a characteristic difference in auxiliary coil data: as described in **Section 4.2.2**,

variance is concentrated in the first few principal components when EMI is present, whereas thermal noise in the absence of EMI distributes variance more uniformly across principal components. To quantify this, we defined ρ_1 as the percentage of total variance explained by the first principal component relative to the cumulative variance of all principal components derived from auxiliary coil data. Frames with ρ_1 exceeding a threshold of 95% were classified as "EMI-contaminated" and processed by the AES module; frames below this threshold bypassed AES to preserve original signal integrity.

As noise decorrelation (ND) using pre-scan noise covariance measurements⁹⁸ is a standard phased-array MRI reconstruction step for maximizing the signal-to-noise ratio (SNR), we compared two pipelines: (1) "Baseline" reconstruction, which applied ND only (no AES), and (2) "Proposed AES" reconstruction, where the AES module was applied after ND. In both pipelines, we performed parallel imaging reconstruction using GeneRalized Autocalibrating Partially Parallel Acquisitions¹³⁸ (GRAPPA), followed by adaptive coil combination¹³⁹. The complete AES reconstruction and PRF thermometry pipeline (described in **Section 4.3.2**) is summarized in **Figure 4-1C**.

4.3.2 PRF MR Thermometry

To resolve phase wrapping during the rapid heating, a cumulative complex conjugate-based PRF method³⁵ was performed:

$$\Delta\phi(t) = \sum_{j=1}^t \arg(I_j \cdot I_{j-1}^*) \quad (4-9)$$

$$\Delta T(t) = \frac{\Delta\phi(t)}{\gamma \cdot \alpha \cdot B_0 \cdot TE} \quad (4-10)$$

where ΔT is the PRF map at time frame t , $\arg(I_j \cdot I_{j-1}^*)$ is the conjugate phase difference between two successive dynamic complex images, γ is the gyromagnetic ratio ≈ 42.58 MHz/Tesla, α is the PRF temperature coefficient ≈ -0.01 ppm/ $^{\circ}\text{C}$, B_0 is the main magnetic field strength, and TE is the echo time. Field drift was corrected by fitting a first-order polynomial to a non-heated reference region.

To mitigate respiratory motion artifacts in vivo, an image-navigated multi-baseline method (see details in Chapter 3) for motion-compensated (moco) PRF calculation¹⁴⁰ was implemented. Five distinct motion states were established from the multi-baseline library using an image-based self-navigator, which was extracted from a region of interest (ROI) near the lung/liver interface from the phase image. For the subsequent frames, phase accumulation was calculated relative to the frames from the same motion state:

$$\Delta\phi_{\text{moco}}(t) = \sum_{j \in M(t)} \arg(I_j \cdot I_{j_{\text{prev}}}^*) \quad (4-11)$$

where $M(t)$ is the set of time indices $j \leq t$ belonging to the motion state, $I_{j_{\text{prev}}}^*$ is the immediately preceding frame within the same motion state.

Thermal dosage was calculated using the cumulative equivalent minutes at 43 $^{\circ}\text{C}$ (CEM43) model¹⁴⁴. A threshold of 240 CEM was used to define the ablation zone from tissue necrosis.

4.3.3 MRI-Guided MWA Experimental Setup

The setup of the gel phantom and in vivo pig liver MWA experiments is shown in **Figure 4-2**.

All experiments were performed on a whole-body 3 T MRI system (MAGNETOM Prisma, Siemens Healthineers, Germany). An 18-channel body array coil was used as the auxiliary coil set for EMI detection, while various array coils (e.g., body, spine, flexible) were used as the primary coils for imaging. An FDA-approved 2.45 GHz MWA system (Saberwave ECO-200G, Nanjing ECO Medical Instrument Co., China) was positioned inside the RF-shielded MRI scanner room, just outside the 5-Gauss line. A water-cooled MRI-compatible microwave antenna was connected to the generator via a 5-meter coaxial cable. No hardware modifications were made to the MWA system.

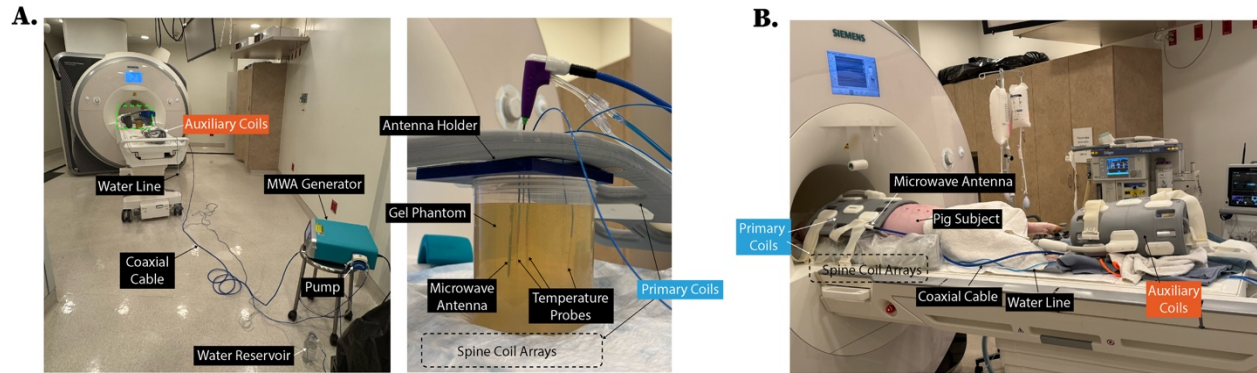


Figure 4-2. Photos of the experimental setup for the (A) gel phantom and (B) in vivo pig microwave ablation (MWA) experiments in the MRI scanner room. Black dashed boxes indicate the integrated spine coils within the patient table. No filters or shielding layers were applied to the MWA system.

The MWA system has four operating modes, each introducing distinct EMI characteristics: (1) *System Off*: system powered off (minimal EMI); (2) *Standby*: Generator on; irrigation pump and ablation off; (3) *Pumping*: Generator and irrigation pump on; ablation off; (4) *Ablation*: active ablation with continuous water circulation.

4.3.4 Gel Phantom Ablation Experiment

A 7.5% w/v gel phantom was prepared by dissolving food-grade bovine gelatin powder (200 bloom) into deionized water at room temperature. The mixture was heated to 60 °C to ensure polymerization and 0.5% w/v sodium benzoate (Sigma-Aldrich, St. Louis, MO) was added as a preservative before cooling.

Prior to ablation, the microwave antenna was inserted to a depth of 70 mm. Three fiber-optic temperature probes (Micronor Sensors, Inc., Ventura, CA) were inserted parallel to the antenna at radial distances of approximately 8 mm, 15 mm, and 50 mm. A 3D T1-weighted dual-echo gradient-echo (GRE) MRI sequence (TR = 4.16 ms, TE = 1.34/2.57 ms, flip angle = 9°, slice thickness = 1.5 mm, in-plane resolution = $1.18 \times 1.18 \text{ mm}^2$) was acquired for antenna and fiber optic probe localization prior to ablation. A single ablation was performed at 50 W continuously for 120 seconds. PRF MR thermometry was acquired using a 2D GRE sequence with GRAPPA (acceleration rate $R=2$) and integrated ACS data acquisition at each time frame.

4.3.5 In Vivo Swine Ablation Experiment

Animal studies were approved by the UCLA Animal Research Committee (ARC 2022-074). Three healthy male Yorkshire pigs (Premier Biosource, Ramona, CA), each weighing 30-40 kg, were sedated and mechanically ventilated (5 sec/cycle). The microwave antenna was inserted percutaneously into the liver parenchyma under ultrasound guidance (iU22, Philips, Netherlands) in the control room by a board-certified interventional radiologist (8 years of experience). The

animal subject was then transferred to the MRI scanner, where a respiratory monitoring unit (PERU 098, Siemens, Germany) was connected to trigger MRI acquisition.

A non-contrast breath-hold 3D T1-weighted dual-echo GRE MRI sequence was acquired for anatomical reference and antenna localization prior to ablation. A 2D GRE PRF thermometry sequence was acquired using GRAPPA ($R=2$). All data were acquired using respiratory triggering at end-expiration to minimize bulk respiratory motion (acceptance window = 20%, delay = 600 ms). The first 20 triggered image frames were acquired prior to ablation to establish a multi-baseline library for suppression of residual motion-induced phase variations. A single continuous (duration 2-10 min) ablation was performed in each subject. The thermometry sequence continued for at least 3 minutes post-ablation to monitor passive heating and cooling. Detailed imaging parameters are summarized in **Table 4-1**.

Following the cooling phase, the 3D T1-weighted scan was repeated to assess the ablation zone geometry based on hyperintense T1-weighted signal changes. Finally, the pig subjects were euthanized, and the liver was explanted for gross pathology analysis along the antenna tract.

Table 4-1. Imaging parameters for MR thermometry during the MRI-guided microwave ablation experiments at 3T. GRE: gradient echo. GRAPPA: Generalized autocalibrating partially parallel acquisitions. R: acceleration rate. FOV: field of view. TR: repetition time. TE: echo time.

	Gel Phantom Ablation Experiment	In vivo Pig Ablation Experiment (N=3)
Sequence	GRE	Respiratory-triggered GRE
Parallel Imaging Acceleration Rate	$R=2$ (GRAPPA)	$R=2$ (GRAPPA)
Number of Primary Coil Channels	12	14, 12, 8
Number of Auxiliary Coil Channels	18	18
FOV (mm ²)	200×200	270×270 , 364×220 , 309×139
In-Plane Resolution (mm ²)	1.56×1.56	1.46×1.46 , 1.72×1.72 , 2.10×2.10
Slice Thickness (mm)	3	4
Flip Angle (°)	8	8
TR (ms)	16	16
TE (ms)	10	10.89, 10.89, 11.52
Bandwidth (Hz/px)	260	260
Temporal Resolution (s/frame)	1.40	1.02
Temperature Map Update Interval (s)	1.40	5

4.3.6 Evaluation

To evaluate the EMI suppression performance, the SNR was calculated as the mean signal intensity within an ROI in the object divided by the standard deviation (SD) of a background ROI outside the imaging object. In addition, the EMI suppression rate η ¹³⁶ was calculated as:

$$\eta = \frac{\sigma_u - \sigma_s}{\sigma_u} \times 100\% \quad (4-12)$$

where σ_u and σ_s denote the background SD before and after AES, respectively. Temporal stability was analyzed by computing the mean and SD of these metrics across dynamic time frames. To evaluate the effect of kernel size on AES performance, η and AES computation time were assessed as a function of kernel size for both the gel phantom and in vivo datasets.

In phantom experiments, PRF-based temperature measurements were validated against fiber-optic temperature probes. A 3×3 ROI centered on each probe tip was averaged to compute the temporal mean absolute errors (tMAE). For in vivo experiments, temperature bias and precision were assessed in non-heated regions by calculating the pixel-wise tMAE and temporal SD (tSD) maps.

The ablation zone predicted by MR thermometry (i.e., CEM43 thermal dose map with a threshold of 240 CEM) was compared with the hyperintense region on post-ablation T1-weighted MRI and gross pathology of the explanted liver.

4.4 Results

4.4.1 Gel Phantom Ablation Experiment

The MWA operating mode was controlled manually in the following order during the MRI acquisition: *System Off* (25 frames), *Standby* (25 frames), *Pumping* (25 frames), *Ablation* (60 frames), followed by a cooldown phase consisting of both *Standby* and *System Off* modes.

Figure 4-3 and **Figure 4-4** illustrate the AES performance during active ablation. Without AES, the MWA system generated broadband EMI spanning the k-space data of all primary coil channels (**Figure 4-4A**), which led to significant SNR degradation in the magnitude and phase images (**Figure 4-3A and 4-3B**). AES substantially suppressed this interference, restoring image quality across all channels, with a median 16.3-fold increase in SNR (up to 23.5-fold) and a median EMI suppression rate (η) of 96.0% (up to 98.3%). The complex difference between the baseline and proposed AES reconstructed images exhibited minimal structured signal, demonstrating that the algorithm effectively removed EMI without compromising the underlying MRI data. Furthermore, the performance was stable throughout the entire ablation procedure, with consistent SNR and η maintained across all time frames during ablation (**Figure 4-3G and 4-3H**).

Figure 4-5 compares channel-combined images using AES across various MWA modes. The EMI characteristics varied across modes, with *Pumping* and *Ablation* modes causing the most severe image degradation. AES consistently restored image quality to a level comparable with the reference frame. This resulted in substantial SNR improvements of 16.9-fold (*Standby*), 37.7-fold (*Pumping*) and 39.8-fold (*Ablation*). Furthermore, AES achieved high EMI suppression rates of 93.8% (*Standby*), 95.3% (*Pumping*), and 95.2% (*Ablation*). The successful restoration of key structural details and MWA-induced signal changes in the gel phantom confirms that AES meets the requirement for accurate monitoring of MWA.

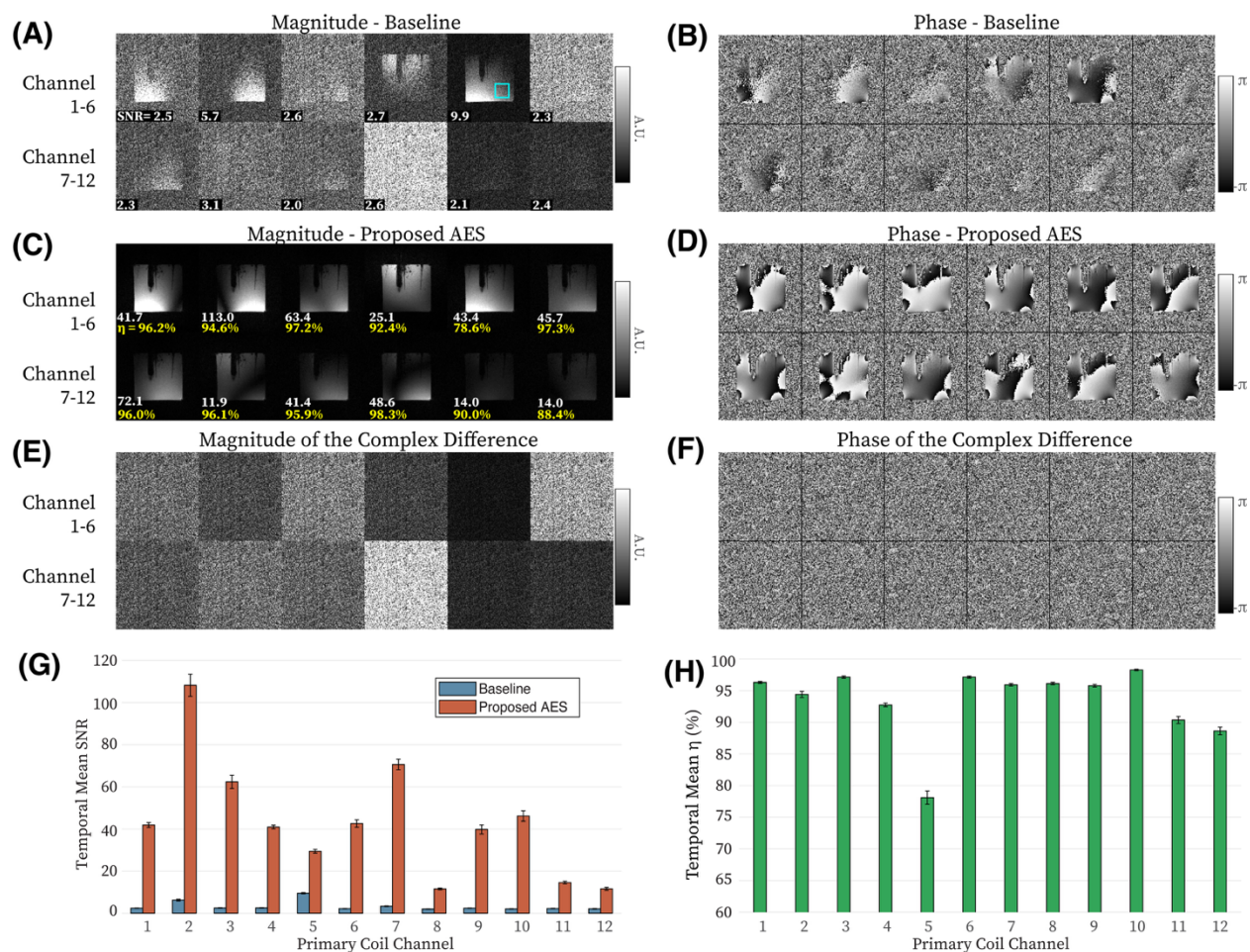


Figure 4-3. Channel-wise AES performance during the gel phantom ablation experiment. **(A, B)** Without AES, magnitude and phase images from each primary coil channel exhibited strong EMI contamination and severe SNR loss. **(C, D)** With AES, the magnitude and phase images demonstrated substantial EMI suppression and SNR improvement in all coil channels. **(E, F)** The magnitude and phase of the complex difference between the images with and without AES showed minimal structures, demonstrating effective EMI suppression without removing desired signals from the imaging object. Rectangular regions placed in a non-heating gel (blue box) and outside the imaging object (not shown) were used to calculate SNR (white text) and EMI suppression rates (η , yellow text). **(G-H)** Temporal mean SNR and EMI suppression rate (η) for each primary coil channel across all time frames during ablation. The error bars represent temporal standard deviations.

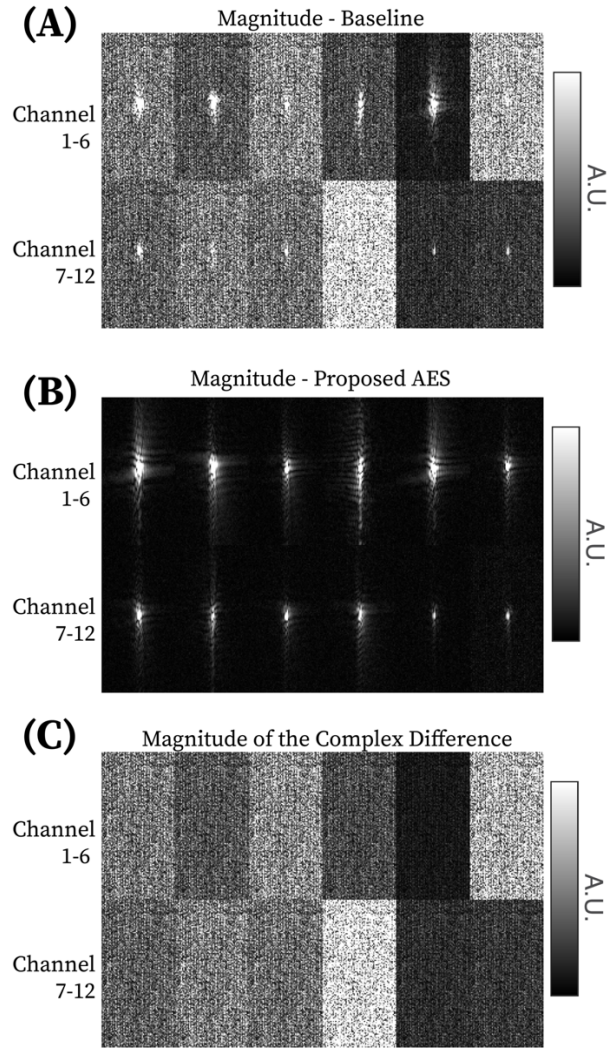


Figure 4-4. k-space magnitude data from all 12 primary coil channels for the same image time frame during the gel ablation experiment shown in **Figure 4-3**. **(A)** Images without AES showed severe EMI contamination across the entire k-space. **(B)** After AES, k-space data showed substantial EMI suppression. **(C)** The magnitude of the complex difference image showed that only EMI was removed.

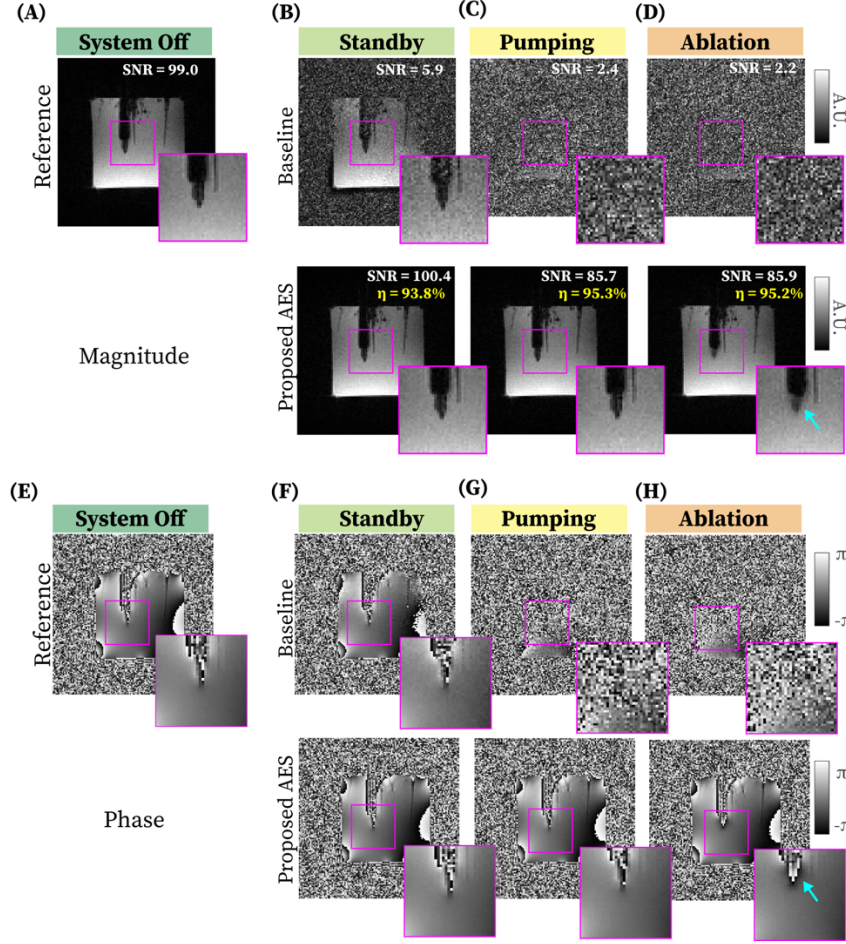


Figure 4-5. Channel-combined MR images after AES demonstrated robust performance for varying levels of EMI in the gel phantom ablation experiment. Representative image frames from four distinct microwave ablation system operating modes are presented. **(A-D)** Magnitude images and **(E-H)** phase images show that AES consistently restored SNR to a high level comparable to what was observed in the *System Off* reference frame (A), regardless of the EMI levels in *Standby*, *Pumping*, and *Ablation* modes. The microwave antenna tip and ablation-induced image signal changes (blue arrows) were clearly resolved with AES, demonstrating the ability to capture signal changes required for MR thermometry. SNR (white text) and η (yellow text) for the selected frames are labeled. SNR was calculated using the same ROI placement as described in **Figure 4-3**.

To validate the pipeline design, **Figure 4-6** compares five reconstruction strategies: uncorrected, ND only (Baseline), AES only, AES followed by ND, and ND followed by AES (Proposed AES). Applying both ND and AES consistently outperformed using either technique alone.

Between the two pipelines that combined ND and AES, applying ND prior to AES consistently yielded higher SNR and EMI suppression across all operating modes, establishing it as the optimal reconstruction pipeline for the subsequent experiments.

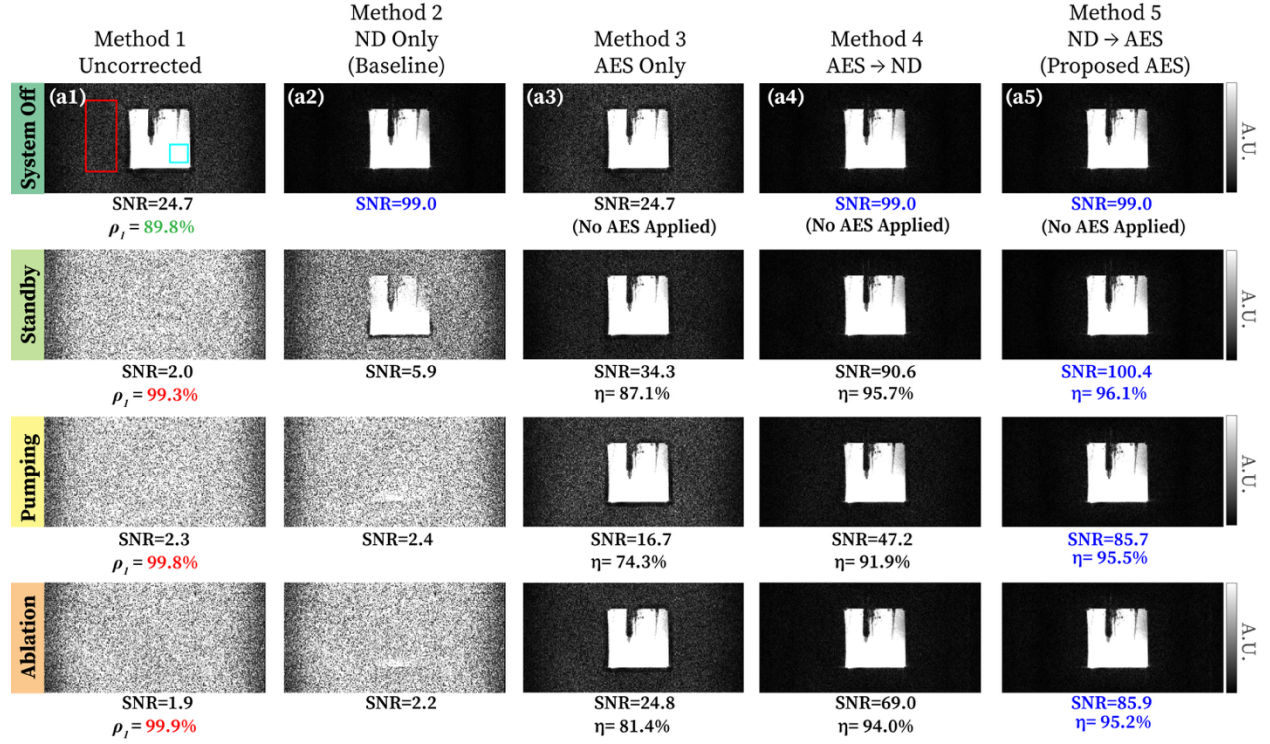


Figure 4-6. Comparison of five reconstruction pipeline configurations across four MWA system operating modes: (a) *System Off*, (b) *Standby*, (c) *Pumping*, (d) *Ablation*. SNR and EMI suppression rate (η) are reported under the images, and the configuration with the best performance is highlighted in blue. Applying both noise decorrelation (ND) and AES improved image quality compared with using either method alone, with the ND→AES pipeline achieving the highest SNR and EMI suppression across all MWA system operating modes. Blue and red boxes indicate the regions of interest selected for SNR and η calculation. ρ_1 is reported for each selected frame, where a threshold of 95% was used to identify frames requiring AES (red: > 95%, AES needed; green: ≤ 95%, bypass AES). Integrated autocalibration signal (ACS) lines for parallel imaging were acquired within each frame; therefore, ACS and imaging data were from the same MWA mode and exhibit a similar ρ_1 .

The impact of AES on temperature monitoring is illustrated in **Figure 4-7**. Without AES, severe EMI artifacts rendered the PRF temperature maps unreliable, particularly during the *Pumping*

and *Ablation* modes. In contrast, AES successfully restored SNR and resolved the ablation zone on temperature maps. **Figure 4-7E** compares the ROI-based PRF temperature measurements against fiber-optic temperature probes, yielding tMAE of 1.39 °C, 0.29 °C, and 0.28 °C at the respective probe locations.

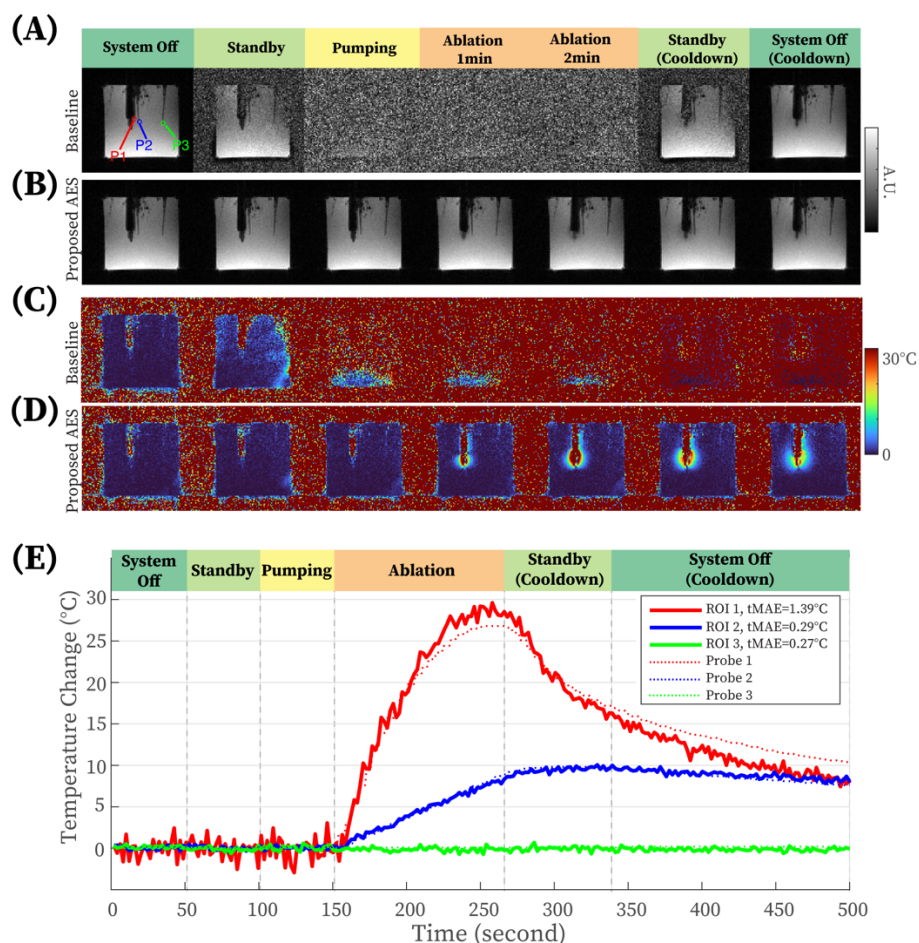


Figure 4-7. Evaluation of continuous PRF thermometry enabled by AES during gel phantom microwave ablation. **(A, C)** Baseline magnitude images and PRF temperature maps, and **(B, D)** those with AES at six representative time points are shown. The strong EMI prevented reliable thermometry with the baseline approach, while the temperature maps with AES clearly resolved the heating and subsequent cooldown. **(E)** Comparison of temperature measurements derived after AES (solid lines) versus three independent fiber-optic temperature probes (dotted lines). The regions-of-interest (ROIs) for PRF measurement are labeled as P1, P2, and P3 in the magnitude reference image (A). The PRF measurements after AES closely tracked the probe readings. tMAE: temporal mean absolute errors.

4.4.2 In Vivo Swine Ablation Experiment

Figure 4-8 and **Figure 4-9** demonstrate the AES performance in an in vivo pig subject during ablation. The EMI exhibited similar broadband characteristics as in the gel ablation experiment, leading to degraded image quality in both magnitude and phase images. AES effectively suppressed these artifacts, yielding a median 3.2-fold increase in SNR (up to 14.7-fold) and a median EMI suppression rate (η) of 70.2% (up to 93.8%). The complex difference between the baseline and proposed AES reconstructed images showed no visible anatomical structures, confirming the effective suppression of EMI while preserving the signal. The SNR and η across all time frames acquired during the ablation mode are summarized in **Figure 4-8G** and **4-8H** and showed a consistent channel-wise performance as the gel ablation experiments.

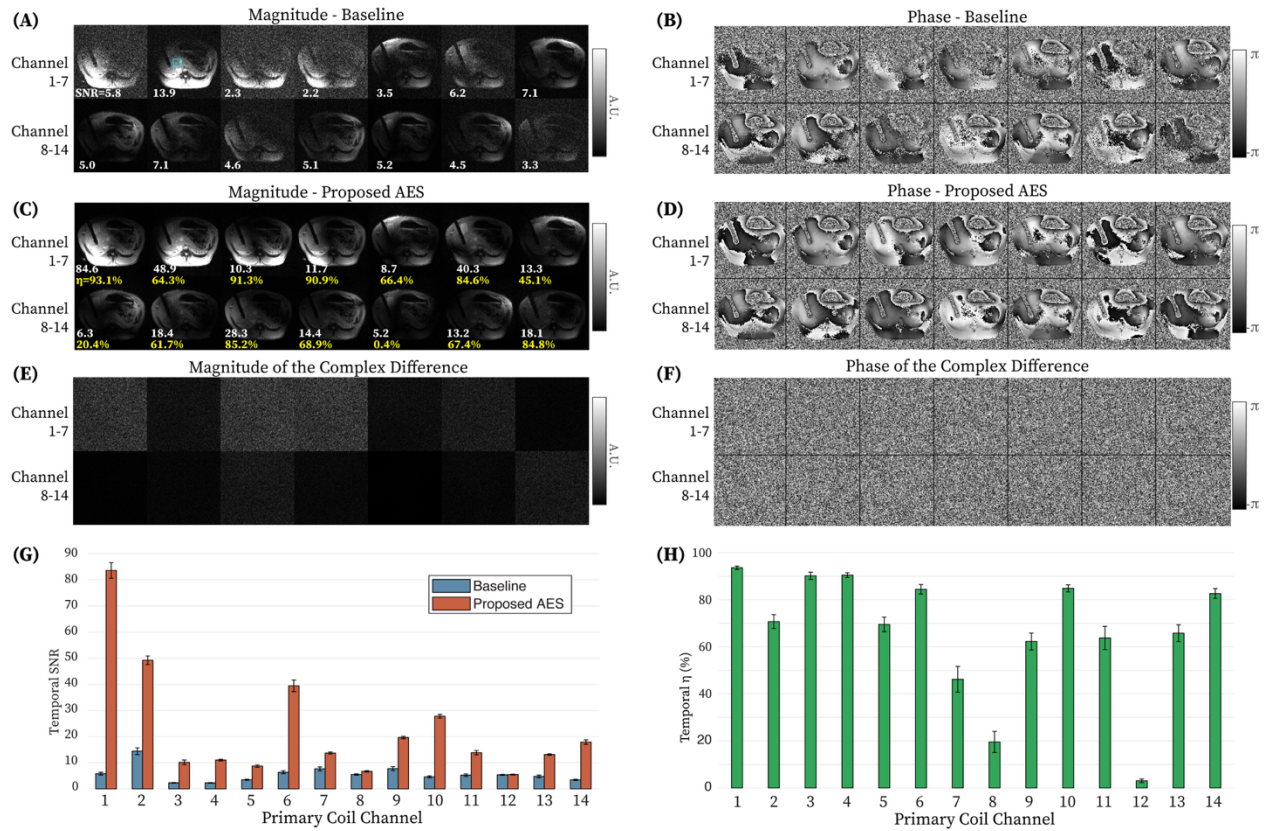


Figure 4-8. AES results in the in vivo swine liver during microwave ablation. **(A, B)** Baseline magnitude and phase images without AES suffered from EMI contamination and SNR loss. **(C,**

D) Magnitude and phase images with AES exhibited substantial EMI suppression and SNR gain. **(E, F)** The magnitude and phase of the complex difference between images with and without AES showed minimal structured signal, demonstrating effective EMI suppression. The blue box in (A) and an ROI outside the imaging object (not shown) were used for calculating the SNR (white text) and EMI Suppression Rate (η , yellow text). **(G-H)** Temporal mean SNR and EMI suppression rate (η) for each primary coil channel across all time frames during ablation. The error bars represent temporal standard deviations.

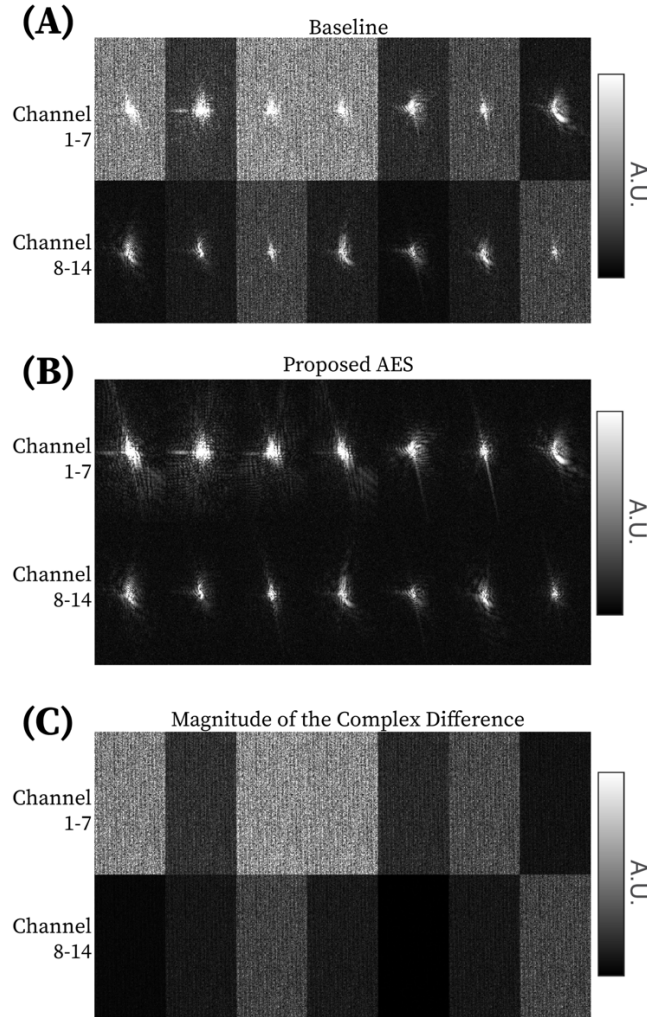


Figure 4-9. k-space magnitude data from all 14 primary coil channels for the same image time frame in **Figure 4-8** in the in vivo swine liver during microwave ablation. **(A)** k-space without AES showed severe EMI contamination, and **(B)** After AES, k-space data showed substantial EMI suppression. **(C)** The magnitude of the complex difference image shows no signal removal, demonstrating effective EMI suppression.

Figure 4-10 shows the channel-combined images using AES across different MWA system operating modes for the same pig subject in **Figure 4-8**. AES successfully enhanced the image quality to a level comparable with the reference frame, with an SNR improvement of 5.5-fold, 7.6-fold, and 13.0-fold, and EMI suppression rate of 81.7%, 87.0% and 92.4% for *Standby*, *Pumping*, and *Ablation* modes, respectively. **Figure 4-11** shows that using multi-channel auxiliary coil data without compression progressively degraded image quality as the number of channels increased, whereas PCA compression achieved the highest SNR and suppression rate. **Figure 4-12** compares the PCA variance distribution of auxiliary coil data between *System Off* and active *Ablation* conditions. During *Ablation*, ρ_1 exceeded 99.9% in both datasets. During *System Off* conditions, ρ_1 was 90.1% in gel and 44.5% in vivo. The $\rho_1 = 95\%$ threshold separated these two conditions in both datasets. **Figure 4-13 and 4-14** show the channel-combined images using AES of two other pig subjects during ablation. In both of these subjects, AES achieved substantial enhancement in image quality with minimal image artifacts, outperforming the baseline reconstruction method.

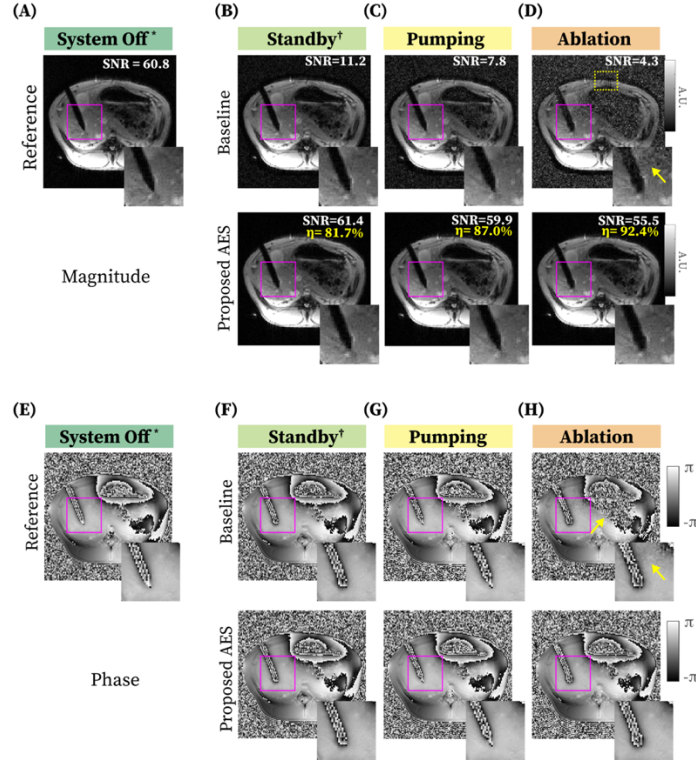


Figure 4-10. (A-D) Channel-combined magnitude images and (E-H) phase images after AES demonstrated robust performance for varying levels of EMI in the in vivo swine ablation experiment. Representative image frames from four distinct microwave ablation system operating modes are presented. The baseline magnitude images suffered from SNR loss due to EMI (yellow arrows), especially during *Pumping* and *Ablation* modes. The yellow box indicates an artifact after coil combination due to the presence of strong EMI. AES consistently restored SNR to a high level comparable to the reference SNR level in the *System Off* mode and effectively suppressed background EMI and EMI-induced imaging artifacts. **System Off* mode data (A and E) were acquired during the cooldown period, after the *Standby* mode. †*Standby* mode data (B and F) were acquired immediately after the ablation.

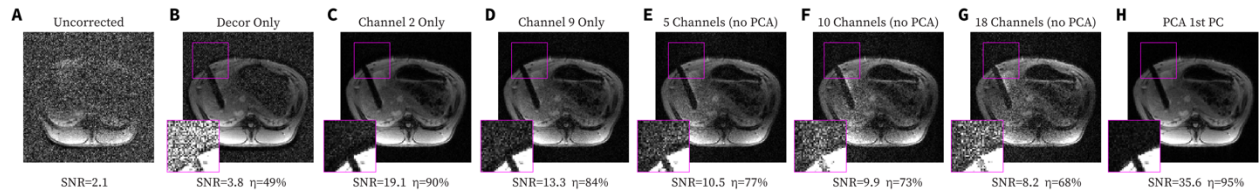


Figure 4-11. (A) Coil-combined magnitude image without noise decorrelation or EMI suppression. (B) Using noise decorrelation but no EMI suppression. (C-D) Using individual auxiliary channels for EMI suppression yields variable performance depending on coil selection. (E-G) Combining multiple auxiliary channels without compression resulted in EMI suppression with progressively degraded image quality. (H) PCA compression extracts the dominant EMI

pattern shared across all auxiliary channels, achieving the highest SNR and EMI suppression rate without requiring manual coil selection. Noise decorrelation was performed in all cases with EMI suppression (C-H).

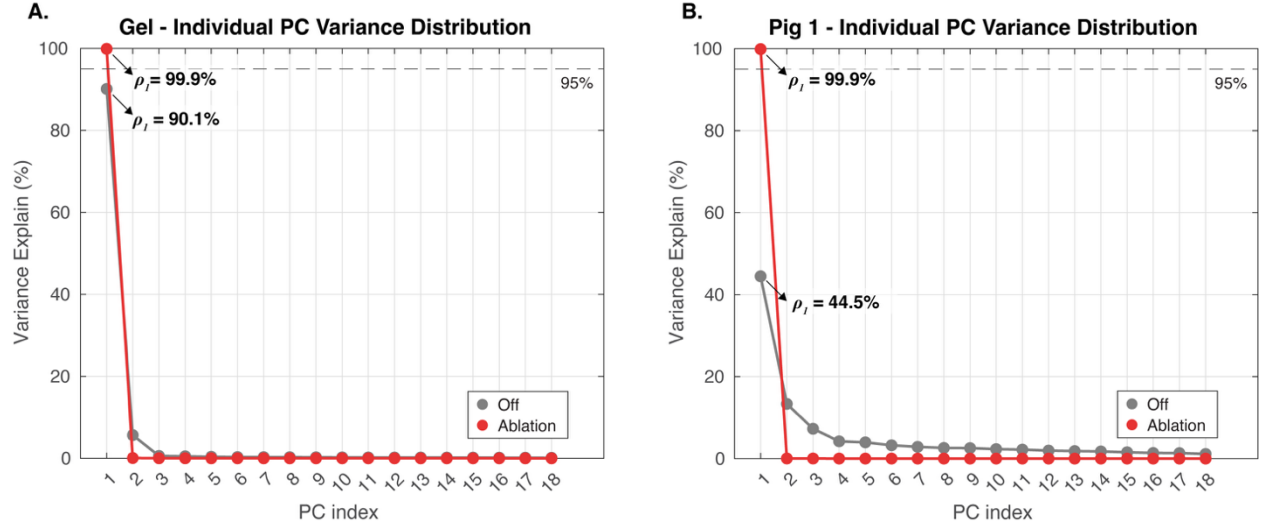


Figure 4-12. Principal component (PC) variance distribution of auxiliary coil data. **(A)** Gel dataset. **(B)** In vivo pig dataset. During ablation (red), ρ_1 exceeded 99.9% in both datasets. During the *System Off* mode (gray), the variance was distributed more broadly across components. The in vivo dataset exhibited a slow decay characteristic of the principal components, with clear separation between *Ablation* and *Off* conditions ($\rho_1 = 99.9\%$ vs. 44.5%). The gel dataset also showed a slower decay during the *System Off* mode, but the separation was less pronounced ($\rho_1 = 99.9\%$ vs. 90.1%), likely due to lower thermal noise levels in the gel phantom. A threshold of 95% was selected to reliably distinguish these two conditions across both datasets. ρ_1 : the percentage of total variance explained by the first principal component relative to the cumulative variance of all principal components derived from auxiliary coil data.

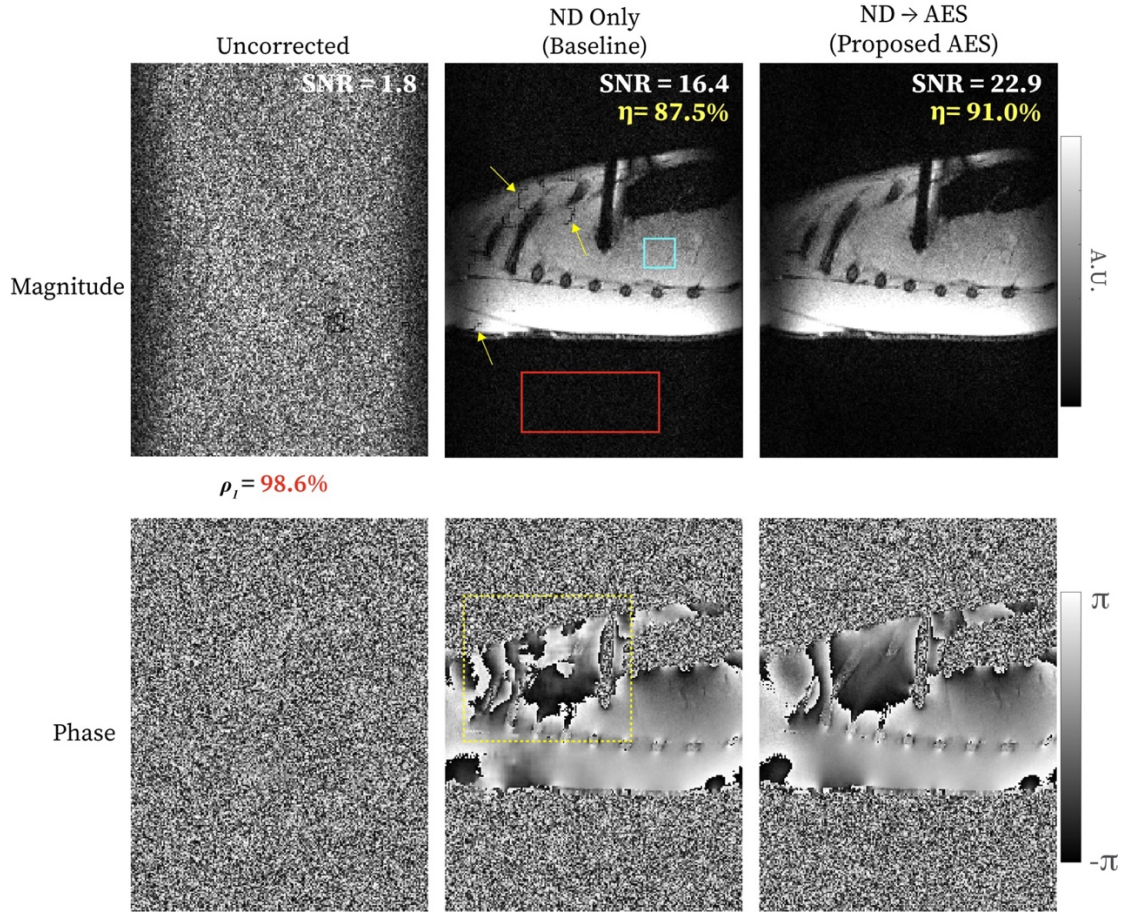


Figure 4-13. AES performance evaluated on channel-combined images in pig subject 2 during ablation. Results from the uncorrected image, the baseline reconstruction without AES, and the proposed AES reconstruction method are compared. Noise decorrelation (ND) alone improved SNR and EMI suppression rate but introduced artifacts in magnitude and phase images (yellow arrows and yellow box) due to residual, unsuppressed EMI affecting the adaptive coil combination. In contrast, the proposed AES reconstruction substantially improved image quality without introducing image artifacts. Blue and red boxes indicate the regions of interest selected for SNR and EMI suppression rate (η) calculation. ρ_1 of the selected frame is reported.

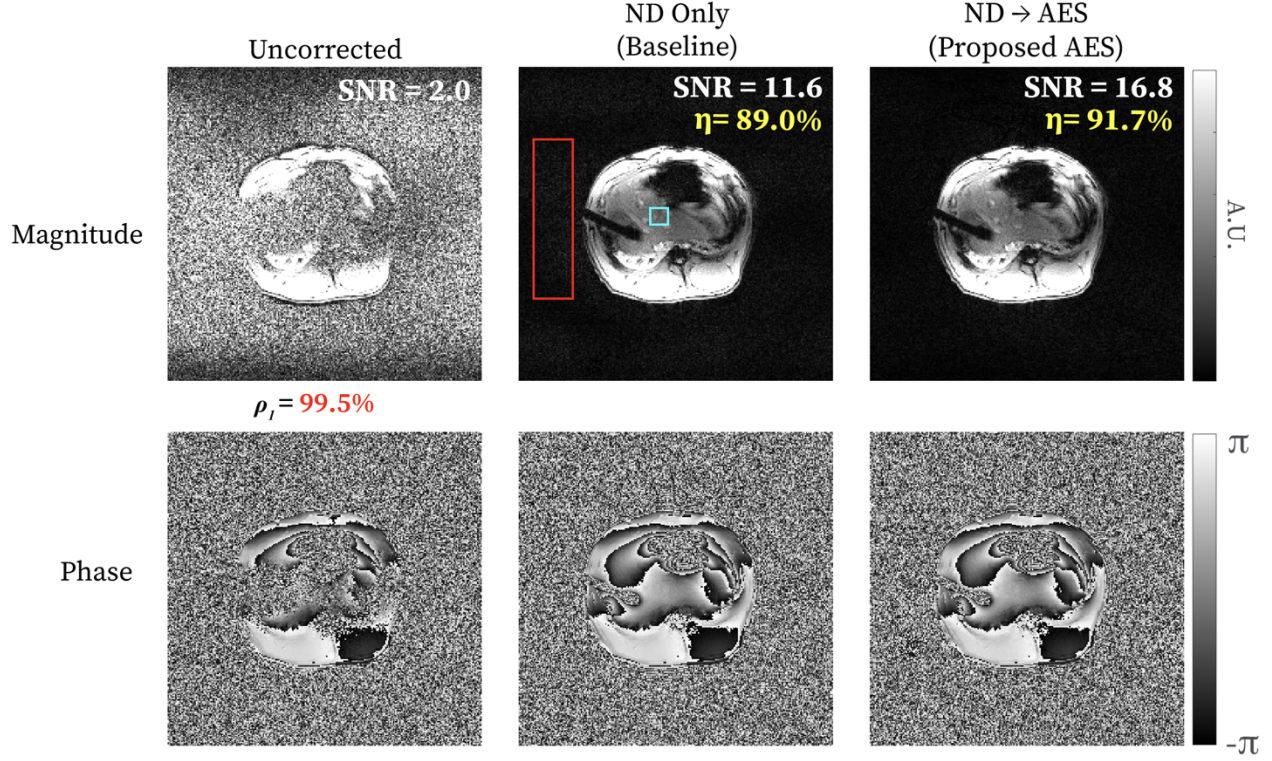


Figure 4-14. Active EMI suppression (AES) performance evaluated on channel-combined images in pig subject 3 during ablation. Results from the uncorrected image, baseline reconstruction without AES, and the proposed AES reconstruction method are compared. Both the baseline and the proposed reconstructions improved the image quality relative to the uncorrected data. The proposed method with AES provided an additional gain in SNR (white text) and a higher EMI suppression rate (η , yellow text). Blue and red boxes indicate the regions of interest selected for SNR and η calculation. ρ_1 of the selected frame is reported.

Figure 4-15 shows the EMI suppression rate and computation time as a function of kernel size L_x . The suppression rate plateaued beyond $L_x \approx 3$ for all datasets while computation time continued to increase. Increasing L_y beyond 1 provided no additional benefit. These results supported our choice to use a fixed kernel size of $L_x=3$ and $L_y=1$ (computation time ≈ 40 ms/frame) for AES in all datasets included in this work.

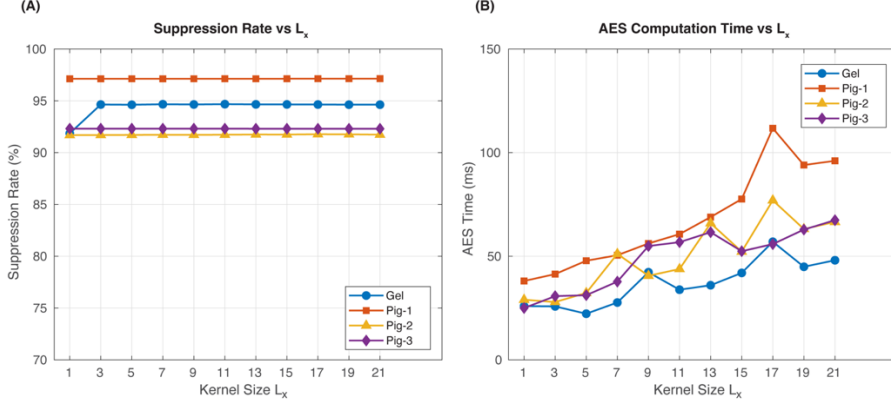


Figure 4-15. Effect of kernel size L_x on AES performance. **(A)** EMI suppression rate (η) and **(B)** AES computation time. A representative frame during active ablation was selected from each of the gel phantom and three in vivo pig subjects. $L_y = 1$ for all cases. Based on these results, the kernel size was set to $L_x=3$.

Figure 4-16 presents the PRF temperature mapping performance with AES during the 10-minute continuous MWA in the same pig subject in **Figure 4-10**. Strong EMI persisted throughout the ablation procedure, causing significant SNR loss, increased temperature fluctuation, and artifacts in the PRF temperature maps. After applying AES, anatomical details became visible, the ablation zone and the antenna path were clearly delineated, and the level of temperature fluctuations was greatly suppressed.

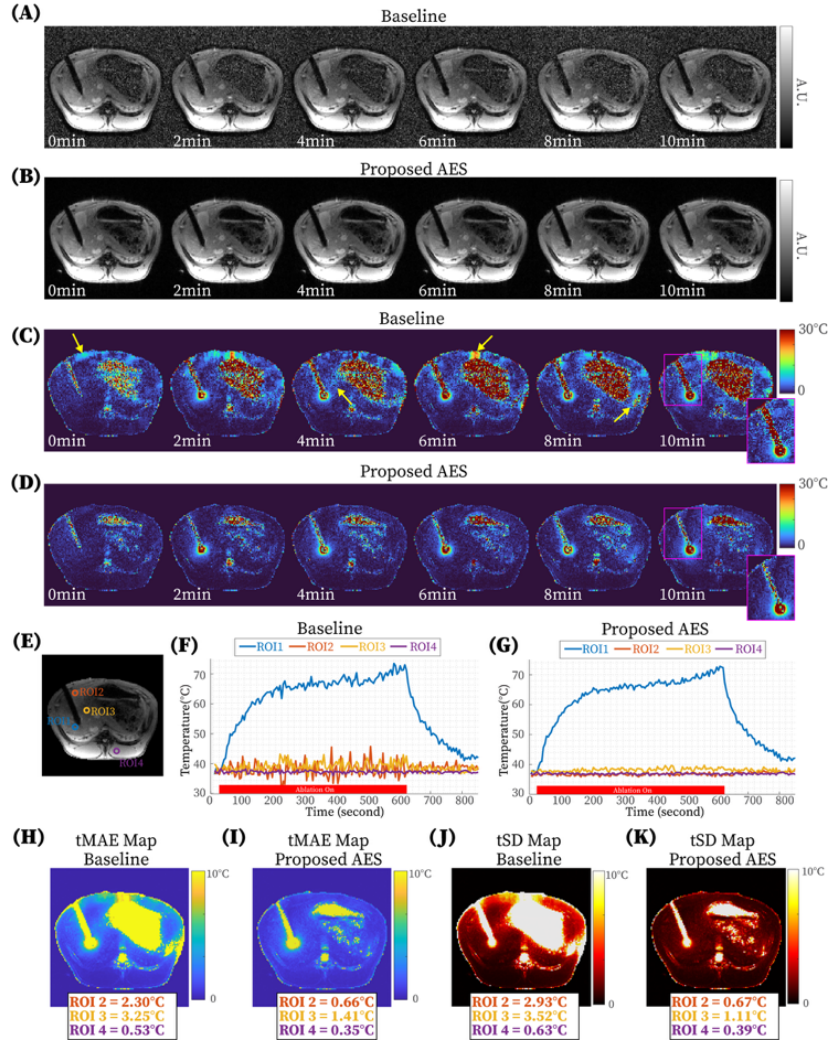


Figure 4-16. AES enabled reliable PRF MR thermometry during microwave ablation in vivo in swine liver. **(A, B)** Magnitude images during the 10-minute ablation without and with AES, shown at 2-minute intervals. AES restored and improved anatomical visibility in the magnitude images throughout the procedure. **(C)** Baseline PRF temperature maps showed EMI-induced temperature artifacts (yellow arrows). **(D)** The PRF maps after AES clearly depicted the localized heating and thermal evolution with minimal temperature artifacts outside the ablated region. **(E)** Locations of four representative regions of interest (ROIs), one from the heating region (ROI1, approximately 10 mm away radially from the antenna) and three from non-heating regions (ROI2, near skin surface along the antenna tract; ROI3: 35 mm away radially from antenna; ROI4, back muscle), where no temperature change should be expected. **(F, G)** Temperature evolution with AES showed that the temperature fluctuations were substantially suppressed in all four ROIs. **(H, I)** Pixel-wise temporal mean absolute error (tMAE) maps with AES showed decreased temperature mapping bias, and **(J, K)** pixel-wise temporal standard deviation (tSD) maps with AES demonstrated improved precision. The tMAE and tSD of three ROIs in the non-heating regions defined in (E) are reported.

Figure 4-17 shows the thermal dose evaluation. AES enabled reliable CEM43 thermal dose mapping, with a clear delineation of the ablation zone and absence of unintended thermal dose accumulation in the non-ablated liver region. The PRF-based thermal lesion was confirmed by 3D T1-weighted MRI (**Figure 4-17C**), acquired immediately after the completion of ablation. The gross pathology of the ablation zone (**Figure 4-17E**) also demonstrated general agreement with the imaging findings.

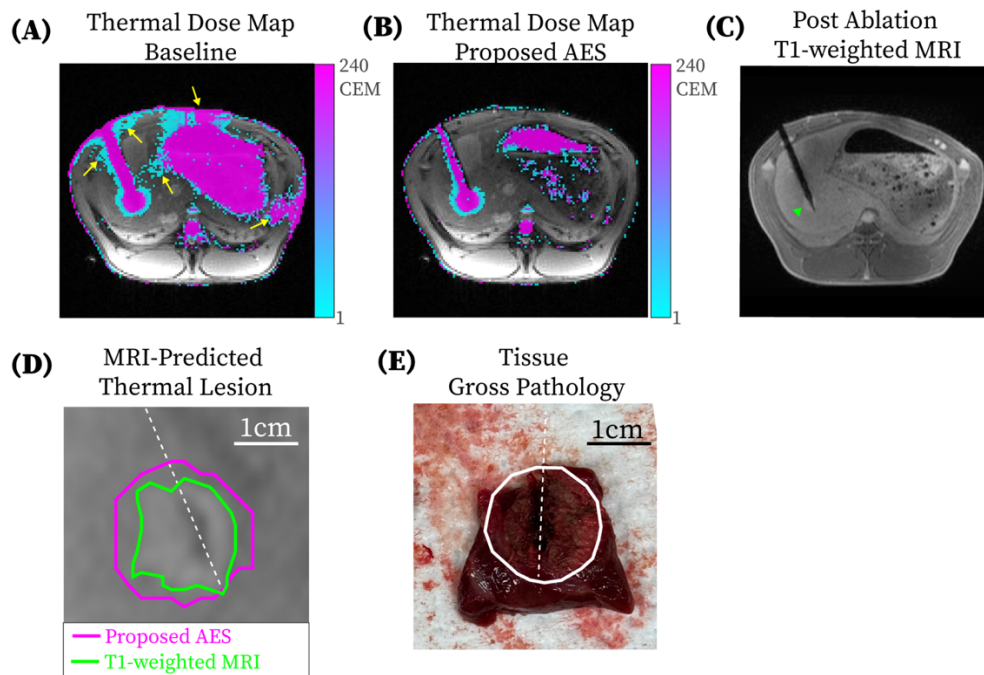


Figure 4-17. PRF-based thermal dose evaluation compared with post-ablation T1-weighted (T1w) MRI and tissue pathology references in the same pig subject. (**A, B**) AES improved PRF thermometry-based cumulative equivalent minutes at 43 °C (CEM43) thermal dose mapping with reduced EMI-related false-positive dose accumulation in non-ablated regions (yellow arrows). (**C**) Post-ablation non-contrast T1w MRI showing the hyperintense ablation lesion (green arrowhead). (**D**) Comparison of thermal lesion boundaries predicted by CEM43 with AES (pink) and post-ablation T1w MRI (green). The white dashed line indicates the antenna path. (**E**) The ablation zone delineated on the explanted liver tissue (white contour) showed general agreement with the predicted thermal lesion boundaries in (D).

4.5 Discussion

In this study, we developed an AES framework designed to address ablation-system-induced interference during MRI-guided MWA on clinical whole-body multi-channel MRI systems. By characterizing and suppressing EMI in the k-space domain, AES substantially improved the image quality in both gel phantom and in vivo pig liver ablation experiments, yielding SNR improvements of 40-fold (gel) and 13-fold (in vivo) and an EMI suppression rate of >92%. Moreover, AES enabled reliable PRF temperature mapping across various MWA system operating modes, maintaining a temperature tMAE <1.4 °C in heated regions and <0.3 °C in non-heated regions relative to fiber-optic temperature probes. These improvements facilitated MRI-based thermal dose estimation with clearly delineated ablation boundaries, which agreed with post-ablation MRI and tissue pathology findings in the pig MWA experiments.

4.5.1 Comparison to Other EMI Suppression Approaches for MRI-Guided MWA

While MRI guidance and MR thermometry offer advantages for hepatic tumor ablation, limited MR-compatible devices and their potential interference with MRI systems remain a key barrier to broader clinical adoption. As reported in our study and by others^{47,51,112,132,134}, EMI from MWA systems corrupts MRI k-space data, obscuring visualization of the microwave antenna, tissue structures, and ablation zone boundaries, thereby increasing the risk of incomplete treatment or collateral thermal damage.

Conventional EMI suppression strategies have primarily relied on hardware modifications or altered ablation duty cycles with intermittent image acquisition. Hardware-based approaches,

such as passive shielding or in-line RF filters^{51,53,132,134}, can attenuate EMI but require customized assembly. This complicates equipment setup, impacts clinical workflow, demands extensive quality assurance for each procedure, and may impede regulatory compliance^{133,135}. Alternatively, intermittent ablation techniques^{47,135} suspend energy delivery during MRI acquisition to mitigate device interference. Although this approach temporarily improves image quality, it inherently disrupts the therapeutic ablation duty cycle, reduces the temporal update rates of thermometry images, and lacks direct image-based monitoring of the effects during actual ablation.

To maintain workflow efficiency without hardware modifications or pausing therapy, a prior software-based technique proposed replacing corrupted k-space lines with data from pre-acquired frames based on empirical thresholds¹³³. However, this data substitution strategy may introduce temperature bias or latency, particularly during rapid heating of MWA. Furthermore, data mismatch (e.g., due to motion) or varying EMI levels can lead to errors because this approach assumes that corrupted data can be replaced, EMI characteristics are consistent, and relies on rigid empirical thresholds.

In contrast, our PCA-based detection module identifies EMI by analyzing the spectral energy distribution of the auxiliary coil data, allowing it to distinguish contamination levels without rigid signal thresholds. Coupled with a frame-by-frame adaptive EMI characterization and modeling scheme, our AES framework automatically accommodates varying EMI conditions and achieves robust EMI suppression and SNR recovery without requiring pre-acquired data or a separate calibration phase.

4.5.2 PCA-Based EMI Detection and Auxiliary Coil Compression

A key component of the proposed AES framework is the use of PCA for both EMI detection and auxiliary coil data compression. We applied AES to multi-channel receiver coil data from phased array coils and a single impulse response function was estimated using the full extent of k-space after PCA compression of the auxiliary channels. Using the full set of auxiliary coil channels with similar physical location directly for EMI modeling introduces redundant degrees of freedom that can degrade the robustness of the kernel estimation. Our PCA-based compression addresses this by extracting only the dominant EMI subspace, which simultaneously reduces dimensionality and suppresses residual MRI signal leakage into the auxiliary coils (**Figure 4-1B**). A comparison of auxiliary coil data processing strategies (**Figure 4-11**) showed that using individual channels yielded variable EMI suppression performance, and increasing the number of channels without compression degraded image quality. PCA compression and extraction of the dominant principal component achieved the highest SNR and EMI suppression rate across all configurations. The per-frame PCA compression of the auxiliary coil data adds approximately 15 ms per time step, which is negligible compared to the overall reconstruction time and is not a bottleneck in the processing pipeline.

As shown in **Figure 4-12**, the auxiliary coil data variance was dominated by a single principal component during ablation, consistent with a single EMI source from the MWA generator. In contrast, *System Off* conditions exhibited a broader variance distribution characteristic of thermal noise, with the in vivo dataset showing a more gradual decay, likely due to elevated thermal noise from the in vivo subject. The $\rho_1 = 95\%$ threshold reliably distinguished these conditions

across both datasets. In settings with multiple EMI sources or varying noise environments, this threshold may need to be recalibrated.

4.5.3 Comparison to Other AES Approaches for MRI and Broader Implications

An effective AES setup for MRI-guided MWA must balance hardware requirements, algorithmic performance, and clinical workflow integration. Our proposed AES framework demonstrates advantages in all three aspects: (1) low hardware cost and complexity for EMI characterization, (2) algorithmic robustness and computational efficiency for multi-channel EMI modeling, and (3) seamless compatibility with standard parallel imaging reconstruction and real-time operation.

Prior AES frameworks have typically relied on dedicated hardware for EMI characterization, such as custom EMI pickup coils¹³⁶, ECG electrodes^{136,137}, or specialized noise-only acquisition windows¹⁴¹ to isolate EMI. While effective for interference characterization, these configurations introduce logistical complexity and require specialized instrumentation. Other studies have used integrated spine¹⁴² or knee coil arrays¹⁴¹ as auxiliary sensors; however, these are either fixed in position or must be docked to the patient table, limiting flexibility during interventional procedures where space on and around the patient table is typically constrained by cables, devices, and monitoring equipment. In contrast, our AES setup uses a standard 18-channel flexible body array positioned at the foot of the patient bed (**Figure 4-2**). This configuration requires no custom EMI sensors, uses existing MRI scanner equipment, and can be freely repositioned, including off the patient table, without disrupting the interventional workflow.

A small kernel size ($L_x = 3$, $L_y = 1$) was sufficient to achieve stable EMI suppression rates exceeding 92% in both gel and in vivo datasets; larger kernels and $L_y > 1$ provided no additional suppression benefit, consistent with previous findings using model-based AES at low field¹³⁶. Additionally, unlike clustering-based approaches that estimate separate transfer functions for different k-space subsets to handle multiple co-existing EMI sources¹³⁶, our framework uses a single transfer function per image time frame. This is well-suited when one dominant EMI source is present, as in MWA with broadband characteristics, and the clustering provided limited additional benefit in this setting. Temporal variations between frames, such as generator mode switches, are instead accommodated through frame-by-frame kernel updates. Together, these design choices enable a processing time of <40 ms per image time frame including PCA compression in MATLAB, compatible with real-time latency requirements for MRI-guided procedures.

Deep learning-based EMI suppression methods have also been proposed, using nonlinear models to either replace the linear kernel fitting¹⁴³ or directly predict EMI-free signals without explicit EMI characterization¹⁴¹. While these approaches have shown promising results, they require a separate training dataset collected prior to the target application. In contrast, our method requires no pre-training; the kernel is estimated on-the-fly from simultaneously acquired auxiliary coil data, making it inherently adaptive to changing EMI conditions within a scan session and well suited for dynamic imaging applications such as real-time MR thermometry.

Another practical advantage of our AES framework is its seamless compatibility with standard multi-channel MRI reconstruction modules, such as noise decorrelation (ND) and parallel

imaging. Because AES operates in the k-space domain, it can be integrated directly into existing parallel imaging reconstruction pipelines without requiring architectural changes to the reconstruction framework and can be readily integrated into vendor reconstruction frameworks or open-source reconstruction platforms¹²² for prospective studies. ND is a standard step to address thermal noise in multi-channel and parallel imaging reconstruction and AES is applied in the same k-space domain. While ND and AES target independent noise sources, the practical effects associated with the order for performing these two steps should be considered. Our results showed that applying ND before AES (ND→AES) yielded the highest SNR and EMI suppression rate across all operating modes (**Figure 4-6**). This is likely because ND first removes static channel-wise noise correlation, allowing AES to more selectively model the remaining structured, time-varying EMI. To minimize potential contamination of the noise covariance matrix by time-varying EMI, we recommend acquiring the pre-scan noise calibration data with the ablation system powered off.

We demonstrated the feasibility of AES in both gel phantom experiments and preclinical in vivo pig liver ablation experiments. Our phantom experiment setup provided a controlled platform for evaluating algorithm performance and thermometry accuracy, while the in vivo experiments confirmed the method's robustness under realistic interventional MRI settings. Beyond MRI-guided MWA, the proposed AES framework may benefit a broad range of MRI-guided interventions, including RF ablation, high-intensity focused ultrasound therapy, laser therapy, and robot-assisted procedures. More robust EMI suppression may also relax shielding constraints in interventional MRI suites, improve the use of intra-procedural communication equipment, and support the integration of additional MRI-conditional tools and monitoring systems.

4.5.4 Limitations

First, this proof-of-concept and technical feasibility study only evaluated the AES performance for MRI-guided MWA in one gel phantom and three pig subjects. Future work should perform experiments on more subjects to evaluate the robustness and inter-subject variability of the AES technique to demonstrate the clinical feasibility. Second, this study evaluated one MRI system, one auxiliary coil configuration, and one MWA system. Additional research is needed to investigate the performance of the proposed AES technique on MRI scanners of different field strengths for different auxiliary coil configurations and ablation systems. Third, the AES framework was implemented offline using a retrospective approach. An inline implementation on the scanner and prospective evaluation would further facilitate the clinical translation.

4.6 Conclusion

We developed and evaluated a model-based active EMI suppression framework that suppresses ablation-device-related interference and enables reliable MRI and PRF MR thermometry during MRI-guided MWA on whole-body MRI systems with multi-channel receiver coils. The method is software-based, operates adaptively on a frame-by-frame basis, and is compatible with existing multi-channel MRI reconstruction. By improving image quality and temperature monitoring without altering existing clinical workflow, this approach could facilitate the broader clinical adoption of MRI-guided MWA and other MRI-guided interventions affected by EMI.

This work has been published in:

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CHAPTER 5 THERMORESPONSIVE POLYMER MODIFIED NANOPARTICLES AND THEIR APPLICATION IN MAGNETIC RESONANCE IMAGING-GUIDED HIGH-INTENSITY FOCUSED ULTRASOUND CONTRAST ENHANCEMENT AT HUMAN BODY TEMPERATURE

5.1 Introduction

Magnetic resonance imaging (MRI) guided high-intensity focused ultrasound (HIFU) is a therapeutic modality that is widely used in the clinic for cancer treatment.¹⁴⁴⁻¹⁴⁶ HIFU can realize precise spatial and temporal control and perform tissue ablation with a focal point of around 1.5 mm³, under the guidance of MRI. Improved MRI contrast would expand the capability of MRI-guided HIFU (MRIgHIFU) to treat detailed tissue structures, for example by better definition of tumor margins or enhancing the location of small tumors.^{29,147,148} In our previous proof-of-concept work^{54,149}, we introduced a “Spotlight MRI” technique that utilized a modulated HIFU intensity in conjunction with nanoparticles that modulated T₁ in response to the stimulation and dramatically increased the signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) of a region of interest. The nanoparticles consisted of mesoporous silica with gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA) chemically bonded and poly(*N*-isopropylacrylamide) (PNIPAm) coated on the outside surface. Mesoporous silica nanoparticles (MSNs) are biocompatible drug delivery platforms and have been applied in MRI contrast enhancement.¹⁵⁰⁻¹⁵² PNIPAm is a thermoresponsive polymer with a lower critical solution temperature (LCST) at 32 °C, and Gd-DTPA is the effective component in the commercialized MRI contrast agent Magnevist[®]. The PNIPAm-functionalized MSNs responded to HIFU-induced temperature modulation around the LCST to alternate water access to Gd-DTPA on the MSN

surface and generate periodic MRI contrast change and enhance MRI contrast around 32 °C. With these functionalized MSNs, the Spotlight MRI technique enhanced the MRI contrast by almost 100-fold.¹⁴⁹

PNIPAm is not best suited to be triggered at human body temperature because its LCST is too low. Therefore, a polymer with an LCST higher than 37 °C is essential for the application of the Spotlight MRI technique in biomedical applications. In addition, the LCST cannot be too high (generally no higher than 45 °C), or hyperthermia may damage healthy tissue.²¹ The LCST of the polymer when it is attached to the particle must be fine-tuned to be at the appropriate biologically relevant temperature.

In this work, we developed polymer-coated MSNs with an LCST of 40 °C optimized to increase and decrease water access to conjugated Gd-DTPA contrast agent by modulating HIFU-induced local temperatures from just below to just above the LCST. First, we describe the over view of the synthesis of POx polymers in order to find one with the desired LCST when attached to the nanoparticles. Second, we demonstrate the MRI contrast enhancement using MRIgHIFU. Finally, we quantitatively compare the enhancements between several polymers and show that our Spotlight MRI methodology achieves stronger enhancement and that the use of the POx polymer with the 40 °C LCST achieves by far the best enhancement versus controls.

5.2 Methods

5.2.1 Overview of synthesis and characterization of POx and functionalized MSNs

The synthesis of P(iPrOx)₂₅-P(BuOx)₄-*t*-SAC (**3**) is as follows: after the simultaneous addition of both monomers (iPrOx and BuOx), the microwave-assisted polymerization was run and terminated with potassium thioacetate (KSAC).¹⁵³ A similar synthetic procedure is followed for simple homopolymer P(EtOx)₅₀-*t*-SAC (**4**). To characterize the LCST of free polymers, temperature-dependent UV-Vis analysis was then performed on polymers solubilized in MilliQ water, as described below. The LCSTs of **3** and **4** were determined to be 40 and 92 °C, respectively. The reversibility of the hydrophobicity change is also supported by UV-Vis analysis over multiple heating and cooling cycles, which showed that the LCST is stable between 40 and 44 °C with an average at 41.9 °C.

After synthesizing POx with the desired LCST, both POx and Gd-DTPA were conjugated to the surface of MSNs. Two POx-functionalized nanoparticles were designed: MSNs-Gd-POx-3, bearing P(iPrOx)₂₅-P(BuOx)₄ (**3**) with an LCST near body temperature, and MSNs-Gd-POx-4, bearing P(EtOx)₅₀ (**4**) as a control to examine whether an appropriate LCST leads to better contrast enhancement. Briefly, Gd-DTPA and a maleimide linker were coupled to amine-functionalized MSNs, and thiol-terminated POx was then attached via thiol–maleimide coupling (**Figure 5-1**). Successful stepwise conjugation was confirmed by FTIR (appearance of the characteristic maleimide and POx peaks, **Figure 5-1c**) and by TGA (increased weight loss after each step), and the Gd-DTPA loading was quantified by ICP-OES (0.89 wt% for MSNs-Gd-POx-3). An additional control conjugated with PNIPAm and Gd-DTPA (MSNs-Gd-PNIPAm)

was prepared following our previous work,¹⁴⁹ to further verify whether an LCST at body temperature yields higher contrast enhancement.

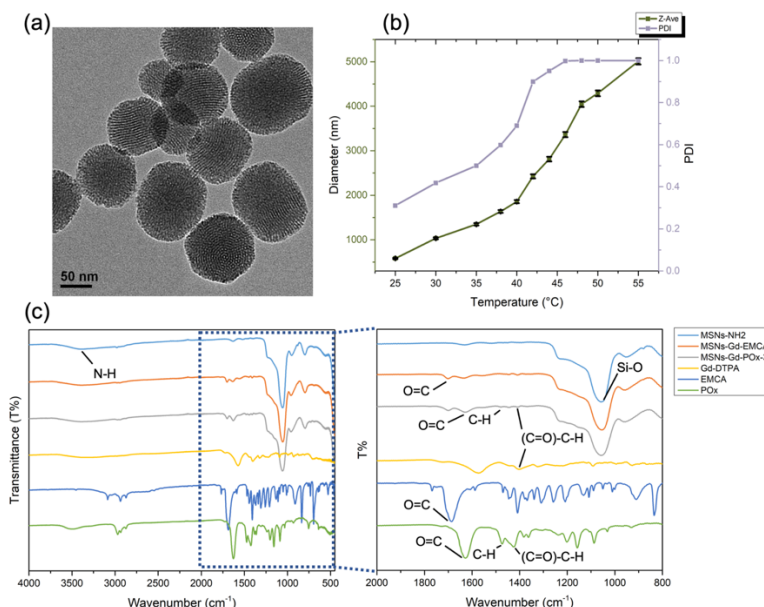


Figure 5-1. Characterization of poly(2-oxazoline) (POx) modified mesoporous silica nanoparticles (MSNs). **(a)** Transmission electron microscopy image of MSNs; **(b)** dynamic light scattering results of MSNs-Gd-DTPA-P(iPrOx)25-P(BuOx)4 (MSNs-Gd-POx-3), where Gd-DTPA is gadolinium diethylenetriamine pentaacetic acid, iPrOx is 2-isopropyl-2-oxazoline, and BuOx is 2-butyl-2-oxazoline; **(c)** Fourier-transform infrared spectroscopy spectra of MSNs at each modification step (left) and zoom in (right).

To characterize the LCST of conjugated POx polymer, we performed dynamic light scattering (DLS) measurements of diluted MSNs-Gd-POx in PBS buffer. The plots of PDI and z-average of MSNs-Gd-POx-3 are shown in **Figure 5-1** (b). The increase of z-average diameter indicates the aggregation of nanoparticles due to hydrophobic POx above LCST, and the increase of PDI indicates wide nanoparticle size distribution caused by their aggregation. Using this method, we can ensure the LCST after conjugation is still in the desired range, which is around 40 °C. The LCST of conjugated **4** is confirmed to be around 65–75 °C using DLS.

5.2.2 MRIGHIFU experiments

Tissue-mimicking gel and MRI-guided HIFU sample preparation

1 g methyl cellulose was slowly added to 15 mL boiled water and stirred for 3 min. Then 25 mL condensed milk was added followed by 10 mL cold water. The mixture was stored in a refrigerator overnight to eliminate air bubbles. 2 mg nanoparticles were dispersed in 0.5 mL water and then mixed with 1 mL gel/milk mixture, resulting in a 1.3 mg/mL nanoparticle gel/milk mixture. The Magnevist (Mgv) control was made in a similar manner and the Gd-DTPA concentration was the same as nanoparticle samples. Mgv was first diluted to 0.5 mL water and then mixed with 1 mL gel/milk mixture. For *ex vivo* tissue experiments, 0.5 mL hemoglobin (0.15g/mL) was mixed with 0.5 mL nanoparticle water dispersion and 0.5 mL gel, resulting in a 1.3 mg/mL nanoparticle gel/hemoglobin mixture and injected in an *ex vivo* beef tissue sample. 17.5 g agarose was slowly added to 500 mL hot water with stirring. Then the solution was heated up to boiling, and then poured into a sample holder mold. After agarose was solidified under room temperature, it was stored in a refrigerator for further use.

MRIGHIFU

All MRI-guided HIFU experiments were conducted using a research-dedicated HIFU system (Image Guided Therapy, Bordeaux, France) integrated with a whole-body 3 T MRI scanner (MAGNETOM Prisma, Siemens Healthineers, Erlangen, Germany). The HIFU transducer used for the phantom experiments was an 8-element annular transducer array with a diameter of 30 mm, frequency of 2.5 MHz, a focal point of $0.7 \times 0.7 \times 3$ mm³ in size, and a peak electrical power output of 80 W. The HIFU transducer used for the *ex vivo* experiments was an 8-element annular

transducer with a diameter of 25 mm, frequency of 1.5 MHz, a focal point of $1 \times 1 \times 5 \text{ mm}^3$ in size, and a peak electrical power output of 80 W.

MRI data acquisition

A golden-angle-ordered 3D stack-of-radial multi-echo spoiled gradient-echo sequence was used to acquire rapid dynamic MRI images. Such a sequence has been demonstrated to provide a balance between spatial and temporal resolution, while still maintaining high volumetric coverage and SNR from our previous study.^{54,154} The data were acquired in the axial orientation with the following parameters: field of view (FOV) = $109 \times 109 \times 18 \text{ mm}^3$, matrix size = $96 \times 96 \times 6$, 4 echoes, $TE_1/\Delta TE = 1.59/1.29 \text{ ms}$, $TR = 7.79 \text{ ms}$, flip angle = 6° .

T1-weighted (T1w) gradient-echo images were acquired with both axial (FOV = $213 \times 213 \times 48 \text{ mm}^3$, matrix size = $192 \times 192 \times 24$, flip angle = 15° , $TE = 2.15 \text{ ms}$, $TR = 4.6 \text{ ms}$) and coronal (FOV = $180 \times 180 \times 64 \text{ mm}^3$, matrix size = $192 \times 192 \times 32$, flip angle = 15° , $TE = 2.15 \text{ ms}$, $TR = 4.6 \text{ ms}$) orientations to locate the natural focal point of the HIFU beam, which was used throughout the experiment without any electronic or mechanical steering.

Image reconstruction

Image reconstruction was performed offline with MATLAB R2017b (MathWorks, Natick, MA). To further improve temporal resolution of our dynamic MRI images and enhance SNR, a k-space weighted imaging contrast (KWIC) filter was applied on the acquired radial k-space data following a sliding window fashion^{92,155}, where the most recently acquired data fill the innermost annulus. Two key reconstruction parameters, temporal resolution (tRes), which stands for the

time to acquire innermost k-space data in a KWIC filter, and temporal footprint (tFp), which stands for the time to acquire the entire k-space data in a KWIC filter, were set to 0.37 s and 10.9 s, respectively, after being carefully optimized based on spatial sharpness⁵⁴. Gridding, 3D density compensation, and coil combination were then performed to reconstruct dynamic images. Details regarding MRI acquisition and reconstruction parameters are listed in **Table 5-1**.

Table 5-1. MRI Acquisition and Reconstruction Parameters

Parameter Name	Parameter Value (Phantom)	Parameter Value (<i>Ex vivo</i> Tissue)
Field of View (mm ³)	109×109×18	180×180×30
Matrix Size	96×96×6	96×96×6
Resolution (mm ³)	1.13×1.13×3	1.875×1.875×5
Flip Angle (°)	6	6
TR (ms)	7.79	7.79
No. TE/TE ₁ /ΔTE (ms)	6/1.59/1.29	4/1.08/1.09
No. of radial angles in the center in a KWIC filter	8	8
No. of total radial angles in a KWIC filter	233	233
Temporal Resolution (s)	0.37	0.37
Temporal Footprint (s)	10.9	10.9

MR temperature measurement

A fast and accurate dynamic temperature measurement is crucial for (1) monitoring if the target temperature during HIFU stimulation is within physiological conditions, and (2) validating the thermoresponsive mechanism of our designed nanoparticles. Proton resonance frequency shift (PRF)-based MR thermometry was used, where the relationship between relative temperature change and MR phase change is described by **Equation 5-1**, where $\phi(T)$ and $\phi(T_0)$ are the phase values at the current time point (during heating) and at a reference time point (before

heating), γ is the gyromagnetic ratio, α is a constant PRF change coefficient = $-0.01 \text{ ppm}/^\circ\text{C}$, B_0 is the magnetic field strength, and τ is the echo time.

$$\Delta T = \frac{\phi(T) - \phi(T_0)}{\gamma \alpha B_0 \tau} \quad (5-1)$$

5.2.3 Spotlight MRI Technique for Contrast Enhancement

The Spotlight MRI technique amplifies the small MRI signal change produced by responsive nanoparticles by deliberately modulating a weak signal at a known frequency so that it can be separated from a static and noisy background by extracting only the spectral component at that frequency^{54,149}. Implementing this principle in MRI requires three elements. First, the stimulus must be periodic. HIFU is delivered with alternative on/off cycles at a fixed modulation frequency, with the power level and the pre-heated baseline temperature chosen so that the local temperature oscillates across the LCST of the polymer rather than rising monotonically. Second, the nanoparticle must convert that temperature oscillation into a reversible T_1 change. Because the polymer layer switches between hydrophilic and hydrophobic states at its LCST, water access to the surface-bound Gd-DTPA is alternately increased and restricted, so T_1 and the corresponding the T_1 w signal intensity follows the HIFU waveform at the same frequency. Third, the MRI acquisition must sample rapidly enough to resolve that oscillation, requiring several image frames within each modulation cycle. The golden-angle-ordered 3D stack-of-radial acquisition with sliding-window KWIC reconstruction described above provides this capability, where the effective temporal resolution sets the sampling rate and the temporal footprint governs the trade-off between spatial sharpness and undersampling artifacts.

The resulting dynamic image series is processed on a voxel-by-voxel basis. For every pixel in the field of view, the T1w signal intensity is plotted against time and a temporal Fourier transform is applied, and the amplitude of the spectral component at the HIFU modulation frequency is assigned to that pixel to reconstruct the modulation enhancement map (MEM). Static tissue, the surrounding phantom, and thermal noise contribute minimal power at the modulation frequency and therefore should be suppressed as the baseline, whereas voxels containing responsive nanoparticles within the HIFU focal zone retain a large spectral peak. The resulting MEM map therefore "spotlights" the stimulated region against a nearly uniform background. Because the spectral amplitude scales with the local temperature modulation, the highest MEM intensity occurs at the focal point. The number of modulation cycles determines the spectral resolution available to isolate the modulation peak and trades directly against total acquisition time. Enhancement is quantified from the MEM relative to the conventional T1w image using CNR and CD% (**Equations 5-2 and 5-3**). Detailed derivations, parameter optimization, and noise analysis of this technique are provided in our previous work^{54,149}.

5.3 Results and Discussion

5.3.1 Polymer Design and Synthesis

A promising thermoresponsive polymer with a tunable LCST is poly(2-oxazoline) (POx). POxs are peptidomimetic polymers and can be synthesized via a controlled ring-opening polymerization.¹² The molecular structure of POx is similar to that of PNIPAm, and like PNIPAm, POx can transit from a hydrated soluble state (coil) to an aggregated insoluble state (globule) across the LCST. The LCST of POx can be tuned by modifying the architectures of

side-chains and/or copolymer composition.¹⁵⁶ The hydrophilicity difference of the side-chain has a large impact on the LCST. Derivatives of 2-ethyl-2-oxazoline (EtOx) exhibit LCSTs from 60 to 100 °C, and derivatives of (2-isopropyl-2-oxazoline) (iPrOx) exhibit LCSTs from 45 to 50 °C.^{156,157} In addition, the POx polymers can be end-capped with various functional groups and thereby conjugated onto nanoparticle surfaces. Therefore, we chose to pursue EtOx- and iPrOx-containing polymers such that the LCST could be tailored by polymer structure and architecture. The POx with fine-tuned LCST was synthesized starting from poly(2-isopropyl-2-oxazoline) (PiPrOx, **2**), a structural analogue of PNIPAm (**1**) with an LCST of around 45–50 °C,^{158,159} as shown in **Figure 5-2**. The copolymer ratio of monomer was varied to modify the LCST and eventually we chose to pursue a P(iPrOx)₂₅-P(BuOx)₄ (**3**) scaffold end-capped with a thioacetate functionality for eventual thiol-maleimide coupling to MSN surfaces as shown in **Figure 5-2**. Additionally, homopolymer poly(2-ethyl-2-oxazoline) (PEtOx, **4**) end-capped with thioacetate was included as a control polymer with an LCST far above physiological temperature. The LCSTs of **3** and **4** were determined to be 40 and 92 °C by temperature-dependent UV-Vis analysis (see detailed characterization in Methods section and Appendix).

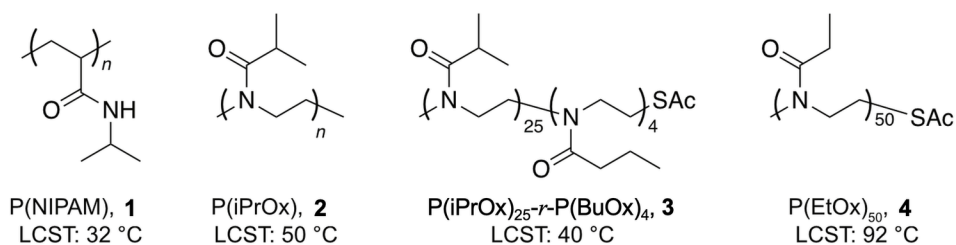


Figure 5-2. Molecular structures of PNIPAm and POx polymers. Variations in the hydrophilicity of the side-chain significantly change the LCST.

Both polymer **3** and **4** were conjugated to MSNs and the resulting nanoparticles were characterized by transmission electron microscopy (TEM), Fourier-transform infrared spectroscopy (FTIR), thermogravimetric analysis (TGA), and ICP-OES (see Methods section and Appendix for details). The LCST after the conjugation of P(iPrOx)₂₅-P(BuOx)₄ to MSNs was characterized by dynamic light scattering (DLS) to be around 40 °C.

5.3.2 Quantification of HIFU-Modulated MRI Contrast Enhancement using POx Polymers

The POx modified MSNs were tested for their contrast enhancement capability under MRigHIFU. The nanoparticles were dispersed in tissue-mimicking gel and milk, and placed in wells inside agarose test objects (i.e., “phantoms”) as reported in our previous work.¹⁰ The samples were treated with the HIFU sequence shown in **Figure 5-3** (a): a 25 s warm-up followed by 10 cycles of 5 seconds on, 5 seconds off (0.1 Hz) modulation, both at 50% amplitude (power of 20 W). The warm-up sequence raised the baseline temperature from room temperature (21 °C) to near body temperature (35 °C), so that a small temperature oscillation in a range of about 3 °C was enough to trigger the reversible contrast change caused by changing water access to the gadolinium compound in the nanoparticles. During the HIFU modulation of MSNs-Gd-POx-**3** shown in **Figure 5-3** (a) right, the temperature increased when the HIFU was on, and the T1-weighted (T1w) signal intensity decreased. This confirmed our hypothesis that when HIFU raises the temperature above LCST, the POx becomes hydrophobic and reduces the water access to the Gd-DTPA on the nanoparticle surfaces and inside nanoparticle pores. The T₁ value increased, leading to the lower T1w intensity. Within the 10 cycles of HIFU modulation, the T1w signal modulation amplitude was constant, which indicated good reversibility of the modified nanoparticles and matched our previous reversibility test result of free POx polymers.

Next, we Fourier transformed the T1w signal intensity over time at every image pixel in the field of view. **Figure 5-3** (b) shows the frequency domain spectrum of the pixel at the HIFU focal point. In the enlarged view shown on the top right, a peak at 0.1 Hz was observed, which is the HIFU modulation frequency. Using this peak intensity, we mapped the modulation amplitude throughout the field of view and reconstructed the modulation enhancement map (MEM) shown in **Figure 5-3** (c). On the MEM, only the pixels that undergo T1w signal change at 0.1 Hz show intensity above the baseline, and from the color map, all of the pixels with enhancement are within the sample area. The pixels at the HIFU focal point have the highest intensities because the temperature modulation is the greatest there and thus it triggers T1w signal changes with the highest amplitude compared to other spatial regions and results in the highest contrast enhancement.

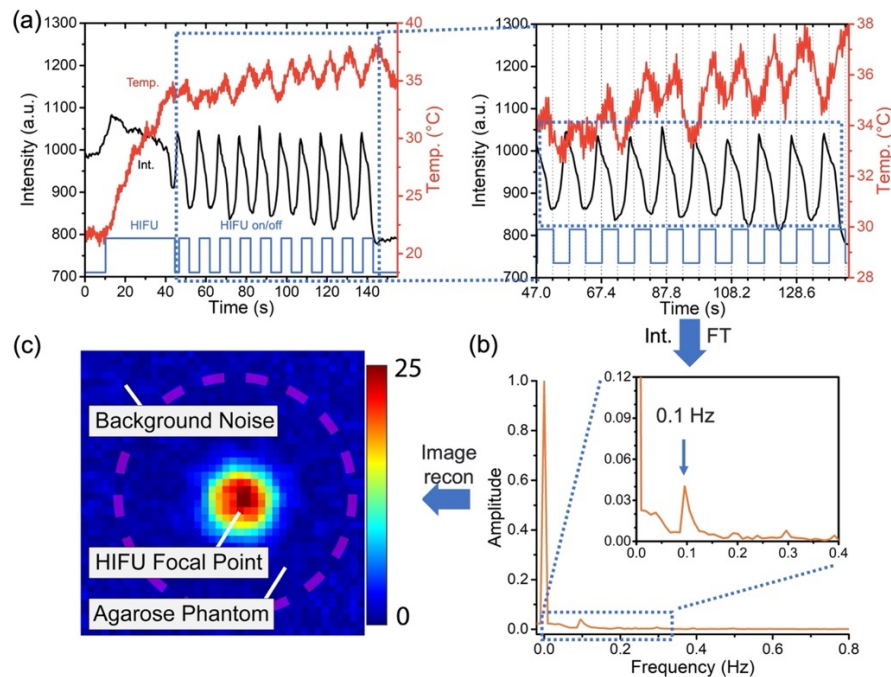


Figure 5-3. (a) Plots of T1w signal intensity and temperature change over time (left) and zoomed-in view of the HIFU modulation time period (right); (b) Temporal Fourier transform (FT) is performed on T1w signal intensity vs. time from (a) to generate Fourier transform

spectrum; **(c)** Reconstructed MEM using the peak intensity of the spectral component at the HIFU modulation frequency for each pixel location (MEM displayed in color scale).

In a second series of studies, the MSNs-Gd-POx-**3** nanoparticles were tested in an *ex vivo* beef tissue sample, a biological and inhomogeneous environment. The nanoparticles were mixed with hemoglobin and injected into the muscle tissue. The HIFU was focused on the injection site using a T1w MRI localizer scan. The same HIFU sequence that was used with the studies in the phantom was used with the beef tissue. The MEM analysis showed that enhancement occurs at the HIFU focal point region for the same reason as the enhancement in the phantom studies. After comparing the MEM with the T1w images, we showed that our Spotlight MRI technique could be applied to a localized area without affecting nearby tissue (**Figure 5-4**). The control was treated with the same HIFU sequence at HIFU focal point to compare the contrast enhancement caused by HIFU-induced temperature oscillation without nanoparticles. To quantify the enhancement, we calculated the contrast-to-noise ratio (CNR) using **Equation 5-2**. In this experiment, the region of interest refers to the HIFU focal point, and the reference area is the beef tissue without HIFU treatment. The higher the CNR the stronger the enhancement. The CNR of HIFU focal point on MEMs of tissue with nanoparticles is almost 5 times higher than the counterpart without nanoparticles, which demonstrates that MSNs-Gd-POx-**3** can enhance T1w contrast in *ex vivo* tissue.

$$\text{CNR} = \frac{|\text{Intensity of region of interest} - \text{Intensity in reference area}|}{\text{Background noise standard deviation}} \quad (5-2)$$

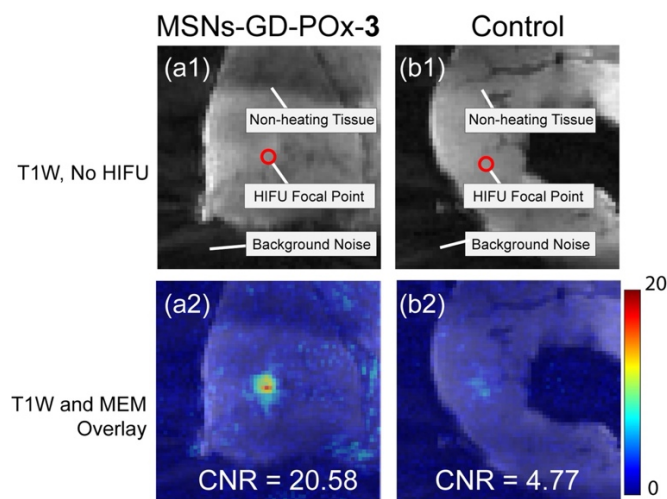


Figure 5-4. T1w images **(a1)** and overlay of T1w images and MEM **(a2)** of beef tissue and that of control respectively **(b1, b2)**.

5.3.3 Quantitative Measurements of Enhancement and Comparisons between Polymers

The overlays of the T1w image and the MEM (displayed in a color scale) of the samples and controls in tissue-mimicking gels are shown in **Figure 5-5**. The components are (a) MSNs-Gd-POx-3, (b) Magnevist (Mgv) control, (c) MSNs-Gd-POx-4, and (d) MSNs-Gd-PNIPAm.

Magnevist is a commercial T_1 contrast agent, and the Gd-DTPA concentration in Mgv was the same as that in MSNs-Gd-POx-3. In the overlay with the T1w image, both the outline of the target object (agarose phantom) and the contrast enhancement at the HIFU focal point from the MEM are shown. With the same color scale, we can observe that MSNs-Gd-POx-3 shows the highest enhancement in the sample region. The three-dimensional plots of the MEMs are shown below the corresponding T1w images.

Similar to the *ex vivo* experiment, we calculated CNR using **Equation 5-2**. In this experiment, the region of interest refers to the HIFU focal point, and the reference area is the agarose

phantom. The CNR of the MEM of MSNs-Gd-POx-**3** is 39.93, which is 8.1-fold higher than that of its T1w image (CNR = 4.94). MSNs-Gd-POx-**3** also shows better enhancement compared to the two polymer control samples: its CNR is 3.2-fold higher than the CNR of MSNs-Gd-POx-**4**, and 2.4-fold higher than MSNs-Gd-PNIPAm. The two control samples with nanoparticles resulted in lower enhancement because their LCSTs are either higher or lower than the HIFU modulation temperature, hence the hydrophobicity of the majority of the polymers on nanoparticles does not change, and thus the contrast change is not significant. The results show that POx-**3** with its LCST at human body temperature is essential to obtain a high enhancement fold at body temperature compared to those of POx-**4** and PNIPAm, which have LCSTs well above and below body temperature respectively. The Mgv control causes a CNR of 11.52 and a 10.5-fold enhancement compared to its T1w image (CNR = 1.10), which indicates that our Spotlight MRI technique can occur from the thermal effect of HIFU on Mgv molecules without nanoparticles. However, the enhancement fold of MSNs-Gd-POx-**3** is 3.5-fold higher than that of the Mgv control, which means our functionalized nanoparticles can further amplify the T₁ modulation range and yield a higher enhancement fold.

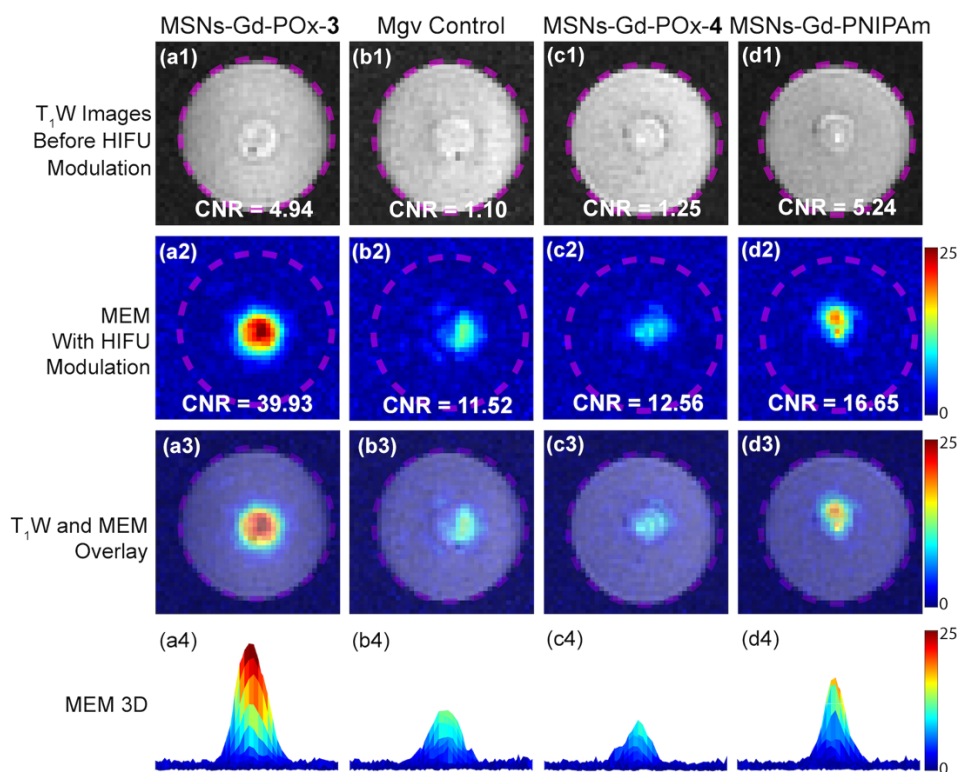


Figure 5-5. T₁w image, MEM, and overlay of MEM and T₁w image of (a) MSNs-Gd-POx-3, (b) Mgv control, (c) MSNs-Gd-POx-4, and (d) MSNs-Gd-PNIPAm and their 3D MEMs respectively. All images were acquired at human body temperature to eliminate contrast difference due to temperature difference. The HIFU-focal point in (a) shows the highest enhancement (red) whereas other samples and controls only show weak enhancement at HIFU focal point (yellow or blue).

An alternative way to present the contrast enhancement of HIFU focal point compared to background agarose gel phantom is to calculate contrast difference % (CD%) using **Equation 5-3** as mentioned in our previous publication⁷. Here the region of interest refers to the HIFU focal point, and the reference area is the agarose phantom. This way can be clinically relevant as physicians focus more on the contrast enhancement of tissue at the HIFU focal point compared to the surrounding tissue. The CD% of the MEM of MSNs-Gd-POx-3 is 22.07, which is 139-fold higher than that of its T₁w image (CD% = 0.16). The CD% enhancement fold of MSNs-Gd-POx-3 MEM compared to that of the three control samples is similar to that for CNR: it is 3.3-

fold higher than MSNs-Gd-POx-4, 3.0-fold higher than MSNs-Gd-PNIPAm, and 3.6-fold higher than Mgv control.

$$CD\% = \frac{|Intensity\ of\ region\ of\ interest - Intensity\ in\ reference\ area|}{Intensity\ in\ reference\ area} \quad (5-3)$$

5.4 Conclusion

In this work, we designed and synthesized a POx polymer with a desired LCST at 40 °C, and functionalized MSNs with POx and Gd-DTPA to realize reversible MRI T₁ contrast change with periodic HIFU modulation. We demonstrate that MSNs-Gd-POx-3 applied with our Spotlight MRI technique is able to achieve image contrast enhancement at human body temperature (37 °C) within a small temperature oscillation range (3 °C) and in a relatively fast data acquisition time (100 s). The contrast difference is 139-fold higher than that of the T1w image, 3.5-fold higher than Mgv, and also higher than MSNs modified with polymers with LCST higher or lower than human body temperature, proving that the tailored LCST is essential to generate significant contrast enhancement. This nanoparticle design brings the Spotlight MRI technique closer to clinical translation as it can work at human body temperature, and it is promising for biomedical applications such as the detection of small tumors or tumor margins.

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modulated contrast enhancement at human body temperatures. ACS Applied Nano Materials. 2025;8(47):22835–22844. doi:10.1021/acsanm.5c04320. († equal contribution)

CHAPTER 6 CONCLUSIONS AND RECOMMENDATIONS

6.1 Summary of Contributions

MRI is firmly established as an integral part of diagnostic imaging in modern clinical care, and its therapeutic role, including in guiding minimally invasive thermal therapies, is increasingly recognized. Across the thermal therapy workflow, MRI supports treatment planning through its excellent soft-tissue and tumor contrast, real-time monitoring by visualizing the interventional applicator and mapping temperature and thermal dose via MR thermometry, and evaluation of treatment outcome after therapy. Despite the promise and demonstrated feasibility, clinical adoption of MRI-guided thermal therapies remains limited to a few large academic medical centers, constrained both by technical challenges, such as physiological motion, lengthy scan times, and limited sensitivity and specificity, and by accessibility barriers, such as specialized hardware and unique skill sets. In this work, we developed multiple techniques that address these barriers across the planning, monitoring, and evaluation of MRI-guided thermal therapies.

Chapter 2 developed a computational modeling framework for MWA with MR thermometry validation. We demonstrated that this joint computational–experimental framework can evaluate microwave energy-delivery strategies to optimize MWA therapy.

Chapter 3 developed a volumetric MR PRF thermometry framework for moving organs, combining stack-of-radial MRI, image-based motion tracking, and image-navigated multi-baseline PRF thermometry. We demonstrated that the framework achieved volumetric PRF

temperature monitoring in moving tissue with high spatiotemporal resolution, accurate temperature measurement during HIFU ablation, and near-full-liver coverage.

Chapter 4 developed an active EMI suppression (AES) technique for MRI-guided MWA that suppresses interference originating from the MWA system without hardware modification. We demonstrated substantial EMI artifact removal and signal recovery for MRI during active MWA, along with reliable in vivo temperature monitoring, without modifying the system or adding shielding layers.

Chapter 5 advanced a contrast-enhancement technique to visualize a novel nanoparticle-mediated agent-delivery platform triggered by MRI-guided HIFU at body temperature. We demonstrated that this nanoparticle contrast amplification technique maximizes MRI contrast across the clinically relevant therapeutic temperature range.

Together, these contributions address key technical and accessibility barriers and advance the planning, monitoring, and evaluation of MRI-guided thermal therapies. Although the techniques presented here were developed specifically for abdominal organs and for MWA and focused-ultrasound therapy, they can be extended to other motion-affected organs, other minimally invasive treatment modalities, and other MRI-guided interventional procedures.

6.2 Future Directions

Several additional directions could further advance MRI-guided thermal therapies. Beyond improvements from the MRI guidance techniques themselves, MRI-guided thermal therapies would also benefit from continued end-to-end software pipeline development, hardware development, and from integration of software and hardware into a unified system to maximize efficiency, safety, and therapeutic outcome.

6.2.1 3D dynamic MR thermometry with active EMI suppression for monitoring hepatic MWA

Microwave ablation offers key advantages for creating larger ablation zones, especially with multiple antennas, and for reaching higher temperatures that help overcome the heat-sink effect. However, these higher temperatures also make MWA more prone to unintended thermal injury and complications if not monitored properly. A 3D MR thermometry framework with volumetric coverage extending beyond the region of interest to the surrounding liver parenchyma, adjacent vessels, and nearby critical structures such as the gallbladder, diaphragm, and bile ducts would therefore be highly valuable for ensuring safety and fully depicting the ablation zone boundary.

In **Chapter 3**, we proposed a 3D thermometry framework and validated it in ex vivo tissue and under non-heating in vivo conditions. In **Chapter 4**, we demonstrated 2D MR thermometry with AES during MWA in vivo. Combining these technologies into a full 3D stack-of-radial MR thermometry pipeline would enable volumetric temperature monitoring and thermal dose evaluation during MWA.

Several additional strategies could further improve MR thermometry performance. One is to employ more efficient MR acquisition and undersampled reconstruction techniques for higher spatiotemporal resolution and volumetric coverage, such as stack-of-spiral MRI with compressed sensing reconstruction¹³⁴, EPI with simultaneous multi-slice acquisition¹⁰⁹, a 3D stack-of-stars EPI sequence¹¹¹, or deep-learning methods that reconstruct directly from undersampled data¹⁶⁰. Complementary PRF thermometry techniques, including MWA-related susceptibility correction^{134,135} and motion-artifact correction¹⁰⁸, can further improve PRF thermometry accuracy and reliability during thermal therapies.

6.2.2 Patient-specific computational model for MWA treatment planning

In Chapter 2, we developed a proof-of-concept computational–experimental framework for MWA treatment planning and validation. There are several directions to further improve the computational models. First, the underlying tissue property coefficients were taken from fixed literature values, which do not account for variation across tissue states or ablation devices and can therefore bias the predicted ablation zone. An inverse optimization framework that calibrates these properties by matching the model-predicted ablation zone to gross pathology could jointly refine the dielectric and contraction coefficients, along with other parameters that vary across subjects and species.

Liver tissue is highly vascularized, and the resulting blood flow and heat-sink effect are major contributors to treatment failure that should be accounted for during treatment planning. In **Chapter 2**, the computational model assumed homogeneous tissue with zero blood perfusion.

For more realistic predictive modeling and addressing the inconsistency in ablation outcome from subject to subject, subject-specific computational models are required.

3D models that represent patient-specific anatomy, including the geometry of the liver parenchyma and vasculature, are crucial for improving the predictive capability of treatment planning. Rather than a 2D axisymmetric geometry, a full 3D geometry should be used, for example derived from a pre-treatment T1w-VIBE sequence with multi-class liver and vessel segmentation via deep learning. The resulting liver and vessel masks can then be imported into the simulation software.

Beyond vascular anatomy, blood flow velocity and direction have been shown to affect ablation outcome and to contribute to the large inter-subject variability. Patient-specific blood flow could be incorporated either through direct quantitative mapping, such as 4D flow MRI¹⁶¹, or through a correction factor derived from its relationship with perfusion biomarkers such as K^{trans} and k_{ep} from dynamic contrast-enhanced (DCE) MRI³³.

Nearby critical structures, including the bile ducts, diaphragm, gallbladder, and obstructing rib cage, could also be incorporated to plan the insertion track. The device insertion trajectory, including insertion direction and depth, should likewise be considered for its effect on ablation outcome.

Finally, tumor-specific geometry and tissue properties could be incorporated, since the tumor environment differs from normal liver parenchyma and vasculature. Each of these factors is a

potential building block toward a full digital twin model for accurate MWA treatment planning. At the same time, incorporating more factors increases model complexity and imposes more stringent validation requirements. The ideal model should therefore balance physiological sophistication against simplicity, with a step-wise refinement strategy preferred. The validation techniques used in this work, MR thermometry and gross pathology from large-animal models (**Chapter 2**) and post-treatment T1w MRI (**Chapter 4**), are potential references for this purpose.

Together, these advances would pave the way toward patient-specific MWA modeling with improved ablation predictability for safer, more effective treatment.

6.2.3 Validation platforms for MRI-guided thermal therapies

Several platforms can be used to validate MRI-guided thermal therapies, including tissue-mimicking gel phantoms, ex vivo tissue specimens, large-animal models, and clinical human patients. Although patients offer the most realistic conditions, such data are scarce, and the clinical environment only permits a limited scope to test new technologies because of safety and regulatory requirements and the tight time constraints of clinical procedures. Preclinical platforms, by contrast, provide a more controlled setting for testing new technologies, with the appropriate choice depending on the stage of technical development.

A range of tissue-mimicking gels have been proposed for therapeutic applications¹⁶²⁻¹⁶⁴. Gelatin is easy to fabricate and readily available, but its low melting point (~35 °C) makes it unsuitable for evaluating thermal ablation. Agarose offers stable physical properties but low optical transparency. Polyacrylamide provides the best optical transparency for visualizing the

coagulation zone and is physically stable, but its fabrication emits toxic precursor (acrylamide) and thus requires a dedicated fume hood. Beyond the gelling material, additives such as BSA, egg white, and thermochromic dyes can be used to tailor thermal, acoustic, electrical, and temperature-sensitive properties, or to introduce a protein-denaturation response, for a specific thermal therapy modality. Future work could pair gel phantoms with programmable motion platforms to reproduce complex and irregular motion patterns beyond the periodic waveform used in **Chapter 3**, enabling systematic evaluation of motion tracking and correction for continuous free-breathing MR thermometry under controlled and repeatable conditions.

Ex vivo tissue specimens, commonly bovine and porcine liver, offer more realistic tissue properties including realistic tissue contraction and protein denaturation, and texture than gel phantoms at comparable cost. However, these same effects can act as confounders and be misinterpreted as imaging or temperature errors, and variability across subject and species should be evaluated when comparing results, whereas phantom fabrication is more reproducible. For validating motion-compensated MRI and MR thermometry, a motion phantom^{140,165} can effectively simulate organ movement. They are also well suited to refining the computational models developed in **Chapter 2**: tissue properties measured from the same specimens could constrain parameter choices in the finite-element model, while effects that are difficult to simulate, such as tissue contraction, water vaporization, and the resulting MWA-induced susceptibility artifacts could be characterized directly and incorporated. In addition, paired temperature measurements and post-treatment histology from the same specimen would support establishing and calibrating thermal dose models for more accurate prediction of tissue damage.

Large-animal models offer the closest approximation to human subjects in size, anatomy, and physiology while still providing a controlled platform for testing of MRI technologies and thermal therapy devices. Healthy animals can be used for feasibility testing, optionally with implanted fiducial markers or artificial targets as landmarks. Their main limitations are longer preparation time, the need for highly skilled personnel, and high cost. Large-animal models are therefore reserved for the stage at which a technique is already robust and must be validated under realistic anatomy, respiratory motion, and perfusion, as in the in vivo swine experiments in **Chapters 3 and 4**. A natural next step is to extend this validation to large-animal cancer models, such as the Oncopig^{107,166} which bear genetically engineered tumors in the pig liver that better represent the true tumor environment.

Small-animal models, most commonly mice and rats, are widely used in preclinical biomedical research to study biological effects such as biodistribution, pharmacokinetics, immune response, tumor microenvironment, toxicity, and survival outcome. They are cost-effective and support large cohorts, providing the statistical power and longitudinal endpoints that larger models cannot practically achieve, and a wide range of established tumor models is readily available. The major limitation of small-animal models is scale, as the much smaller organ size makes testing of clinical interventional devices less realistic, and although dedicated small-animal scanners exist, the different field strength and SNR characteristics do not transfer directly to human imaging and require additional translational effort. Nevertheless, small-animal models provide a crucial intermediate step for research involving combined drug and thermal energy

effects¹⁶⁷, and for the development of nano-theranostic agents such as the HIFU-modulated drug-delivery platform presented in **Chapter 5**.

Together, these platforms offer complementary advantages that map onto different stages of the MRI-guided thermal therapy workflow, from technique characterization to biological validation, and should be selected to match the scope and desired outcome of a given study. A staged strategy that advances a technique from gel phantom to ex vivo tissue to large-animal models, as followed in this dissertation, provides an efficient and rigorous path toward clinical translation..

6.2.4 MRI-guided thermal therapies on high-performance low-field 0.55T MRI

Over the past decade, interventional MRI has largely relied on standard clinical scanners at 1.5T and 3T, used concurrently with diagnostic imaging infrastructure to improve clinical efficiency and maximize scanner utilization. However, the limited bore size of these scanners makes in-bore operation difficult for the physician, and signal voids from the RFA or MWA antenna, or from nearby metal implants, can obscure small lesions and hinder precise ablation margin identification. Dedicated interventional MRI has been developed, most notably open-configuration 0.5T systems developed in the mid-1990s that provided direct physician access to the patient and enabled early applications including neurosurgical resection, biopsy, and MR-guided microwave ablation of liver tumors with intraprocedural monitoring¹³². These systems were ultimately discontinued, as their limited SNR and gradient performance, and inability to share workflow with routine diagnostic imaging which prevented broader clinical adoption. In recent years, low-field scanners (<1T) have been reintroduced and are particularly attractive for interventional MRI, owing to improved field homogeneity, larger bore sizes, and less

pronounced metal artifacts. In particular, a high-performance 0.55T scanner platform with an 80 cm bore has emerged as a sweet spot that balances image quality for diagnostic use with practical access for interventions, and the initial feasibility of MRI-guided thermal therapy applications has been established at this field strength¹⁶⁸.

Realizing this potential toward clinical translation requires further development. The lower field strength brings lower native SNR, and previously established sequence parameters and protocols must be re-validated at 0.55T. More SNR-efficient acquisitions, such as multi-shot EPI or the non-Cartesian approach in **Chapter 3**, could recover SNR without lengthening scan time or degrading temporal resolution, helping to meet the real-time or near-real-time requirements of thermal therapy guidance. In addition, studies characterizing performance across field strengths would facilitate the transfer of MRI technologies from more established platforms to this one. Priorities include evaluating ablation applicator artifacts, characterizing the achievable temperature-to-noise ratio, and profiling the EMI generated by interference-prone systems such as RFA, MWA, and MR-conditional robots, together with the AES technique from **Chapter 4**, so that the accessibility advantages of low-field interventional MRI can translate into broader clinical adoption.

6.2.5 MRI-compatible robotic systems for MRI-guided interventions

Robotic assistance is well established in minimally invasive surgery, where it streamlines procedures and enhances precision and dexterity. It is particularly compelling for MRI-guided interventions, overcoming the ergonomic constraints of in-bore access while reducing the training and operator skill these procedures currently demand, thereby lowering the barrier to

wider adoption. Transferring this technology into the MRI suite, however, faces a critical obstacle: most electronic systems are incompatible with the scanner environment, whether because of ferromagnetic materials, electromagnetic interference with the control system, or artifacts from the interstitial device. To address this, alternative robotic actuation systems, such as hydraulic¹⁰⁶, pneumatic¹⁶⁵, and piezoelectric mechanisms, have been developed to operate within the scanner room. For device-related electromagnetic interference, MR-compatible materials or copper-mesh, Faraday-cage-like shielding can be applied, though at added manufacturing cost and complexity. As demonstrated in **Chapter 4**, our software-driven active EMI suppression offers a further, hardware-free approach to mitigating such interference.

Beyond next-generation robotic hardware, tighter integration of real-time image processing and closed-loop control could drive the robot directly from imaging feedback. Signals such as respiratory motion tracking (**Chapter 3**) and temperature feedback during thermal therapy (**Chapters 3 and 4**) could be incorporated into the control loop to enable motion-compensated tracking and adaptive ablation power adjustment, improving the safety, efficiency, and reproducibility of MRI-guided thermal therapies.

6.2.6 Artificial intelligence for MRI-guided thermal therapies

MRI-guided thermal therapy is a lengthy and iterative procedure in which treatment planning, device targeting, and intraprocedural monitoring each depend on operator experience and on computation and imaging steps that are slow relative to the pace of the procedure. Artificial intelligence offers a way to reduce this burden by providing fast approximations to computationally expensive steps and quantitative support for decisions that currently rely on

experience, which together could improve both the efficiency and the consistency of these procedures.

Before the procedure, the physician plans the insertion trajectory and antenna placement and estimates the resulting ablation zone, often relying on generic protocols or prior experience. The computational framework in **Chapter 2** can provide patient-specific predictions instead, but solving the finite-element model and searching the parameter space remain too slow for clinical use, which restricts the approach to retrospective analysis of a small number of pre-selected protocols. Deep neural networks trained on simulation data¹⁶⁹ or on prior clinical datasets can serve as fast surrogates for these models, exploiting parallelization at inference to predict temperature and ablation-zone probability maps in a fraction of the time. Applied to the simulation library generated in **Chapter 2**, such a surrogate would allow the MWA protocol space of power, duration, and pulsing scheme to be searched far more exhaustively for an optimal treatment strategy, and would make intraprocedural re-planning feasible when the observed heating deviates from the prediction.

During the procedure, device targeting requires repeated breath-holds and moving the subject in and out of the bore, and intraprocedural monitoring demands volumetric imaging at a temporal resolution that conventional acquisition and reconstruction cannot deliver. AI methods can relieve both constraints by accelerating acquisition¹⁷⁰, suppressing undersampling artifacts¹⁷¹, and performing physics-informed quantitative parameter fitting¹¹⁷. This directly addresses the principal limitation identified in **Chapter 3**, where the iterative GRASP reconstruction required approximately 62.5 seconds per slice and confined volumetric thermometry to retrospective use.

A learned reconstruction trained to map undersampled stack-of-radial data to artifact-free dynamic images could provide comparable image quality at inference speeds compatible with real-time monitoring. Learned approaches could likewise improve the phase estimation underlying PRF temperature mapping, increasing precision and robustness in low-SNR or motion-corrupted regions where the current method is least reliable.

6.2.7 Toward clinical translation

The technologies developed in this dissertation, including the computational modeling for MWA treatment planning (**Chapter 2**), volumetric motion-compensated PRF thermometry (**Chapter 3**), active EMI suppression for MRI-guided MWA (**Chapter 4**), and thermoresponsive nanoparticles for HIFU-stimulated contrast enhancement (**Chapter 5**), sit at different distances from clinical use and all require further translational effort along several fronts. First, each technique must be evaluated in larger cohorts to establish statistical significance and reliability. Second, computational cost must be compatible with clinical imaging hardware, and processing latency must be characterized to confirm feasibility within the real-time or near-real-time constraints of the procedure. This can be achieved by reimplementing existing prototyping software pipelines with parallel and GPU computing frameworks. Third, performance should be assessed across an expanded range of hardware platforms and protocols, including different field strengths, pulse sequences, coil configurations, and ablation devices. Fourth, evaluation should extend from pre-clinical and healthy human subjects, which establish safety and baseline performance, to tumor-bearing patients, to confirm that performance is preserved while maintaining tumor contrast, and to subjects spanning a range of body compositions and physiological conditions. Fifth, these techniques must integrate into the procedure without

adding to the visual or cognitive burden of the interventionalist, with intuitive user-centered hardware and software interfaces and end-to-end workflow efficiency characterized directly rather than inferred from component-level gains. Sixth, prospective evaluation against clinically meaningful endpoints, such as technical success, ablation margin adequacy, and local tumor progression, will be required to demonstrate patient benefit beyond technical performance. Finally, collaboration with institutions will be needed to deploy these techniques on commercial scanner platforms and validate them in multi-center studies.

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