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Image-guided Tumor Ablation: Standardization of Terminology and Reporting Criteria—A 10-Year Update[1]

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For the International Working Group on Image-guided Tumor Ablation, Interventional Oncology Sans Frontières Expert Panel, Technology Assessment Committee of the Society of Interventional Radiology, and the Standard of Practice Committee of the Cardiovascular and Interventional Radiological Society of Europe

Image-guided tumor ablation has become a well-established hallmark of local cancer therapy. The breadth of options available in this growing field increases the need for standardization of terminology and reporting criteria to facilitate effective communication of ideas and appropriate comparison among treatments that use different technologies, such as chemical (eg, ethanol or acetic acid) ablation, thermal therapies (eg, radiofrequency, laser, microwave, focused ultrasound, and cryoablation) and newer ablative modalities such as irreversible electroporation. This updated consensus document provides a framework that will facilitate the clearest communication among investigators regarding ablative technologies. An appropriate vehicle is proposed for reporting the various aspects of image-guided ablation therapy including classification of therapies, procedure terms, descriptors of imaging guidance, and terminology for imaging and pathologic findings. Methods are addressed for standardizing reporting of technique, follow-up, complications, and clinical results. As noted in the original document from 2003, adherence to the recommendations will improve the precision of communications in this field, leading to more accurate comparison of technologies and results, and ultimately to improved patient outcomes.

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In 2003, the International Working Group on Image-Guided Tumor Ablation published a document titled "Image-Guided Tumor Ablation: Proposal for Standardization of Terms and Reporting Criteria" (1). At the time, image-guided tumor ablation, and indeed, the subspecialty of interventional oncology, was in its infancy. Nevertheless, it was acknowledged by the members of the Working Group that the new field of image-guided tumor ablation required standardization of terminology and reporting criteria to facilitate effective communication of ideas and appropriate comparison among different technologies. The main objective of the document was "improved precision and communication in this field that leads to more accurate comparison of technologies and results and ultimately to improved patient outcomes" (1). Originally published in 2003 in *Radiology*, the document was subsequently reviewed at regular intervals in conjunction with the Society of Interventional Radiology (SIR) Technology Assessment Committee and republished in near original form in 2005 and 2009. As a testament to its intended utility, this document has been cited by over 600 studies on tumor ablation.

Ten years later, the field of tumor ablation continues to evolve. Tumor ablation modalities that were still being developed at the time of original preparation, such as microwave and focused ultrasound, now have multiple commercially available clinical platforms in routine clinical use (2,3). Newer ablation modalities, such as irreversible electroporation (IRE), have been introduced and clinical niches are being defined (4). Preliminary clinical studies have matured into larger longer-term series with 5- and 10-year follow-up data on par with the surgical and medical oncology literature (5–7). Several randomized, controlled studies have been published or are under way (8,9). Over the interim, our initial document has also given rise to several additional position statements within the field of interventional oncology and been the source for more focused societal statements on tumor ablation of liver, kidney, and musculoskeletal tumors.

Given the number of changes that have taken place in the field of tumor ablation in the past 10 years, the members of the original Working Group and additional interventional oncology experts have taken advantage of the opportunity to meet at the Interventional Oncology Sans Frontiers meeting in Lake Como, Italy, in May 2013 and to incorporate recent advances in this updated document. It is our intention to ensure that this highly utilized standardization continues to remain relevant as it unites all investigators and clinicians practicing interventional oncology by providing a common language to describe therapies and outcomes, develop studies, and communicate with other medical specialties. As was done previously, this document has again been vetted and approved by the Technology Assessment Committee of SIR. In an attempt to attain greater worldwide adoption, this version has also received official approval of the Cardiovascular and Interventional Radiological Society of Europe, CIRSE, and additionally includes more prominent authors from Asia than the initial document.

Scope

The main objective of this document is to improve precision in communication in the field of image-guided tumor ablation, leading to more accurate comparison of technologies, results, and ultimately to improve patient outcomes. Here, we outline a standardized set of terminology to be used and requisite clinical and technical information that should be provided when reporting on tumor ablation. Since our original document, clinical uses and imaging evaluation of tumor ablation have expanded significantly to the point that it is challenging to fully encompass all aspects of tumor ablation in one document. Accordingly, standardization of imaging techniques, imaging findings, and tumor-specific follow-up recommendations will now be reported separately in a companion document. Similarly, despite the authors' commitment to improving all aspects of consensus in the field of interventional oncology, detailed reviews of any specific ablation modality (such as radiofrequency [RF] or microwave ablation) or clinical indication (such as liver or kidney ablation) are beyond the scope of this document.

Classification of Therapies

Image-guided Tumor Ablation

The term **tumor ablation** is defined as the direct application of chemical (ie, nonenergy) or energy-based (ie, thermal and nonthermal) therapies to eradicate or substantially destroy focal tumors (1,10–12). The term "direct" aims to distinguish these often applicator-based therapies from others that are applied orally or via an intravascular or peripheral venous route. The concept of image guidance and planning is emphasized in the title given our radiology perspective and to highlight that imaging (throughout the treatment cycle) is critical to the optimal success of ablative therapies (11,12). Given that most ablative therapies can be performed using a host of imaging modalities (ie, ultrasonography [US], computed tomography [CT], magnetic resonance [MR] imaging, positron emission tomography [PET], and fluoroscopy), the more general term of **image guidance** is preferred, unless a particular

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Abbreviations:
IRE = irreversible electroporation
OS = overall survival
PFS = progression-free survival
RF = radiofrequency
SIR = Society of Interventional Radiology
TTP = time to tumor progression

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imaging modality is mandated as part of the technique. However, virtually all available ablation techniques can theoretically be used with more than one image-guidance modality.

While some have previously referred to these procedures as "minimally invasive" or "percutaneous" therapies, these terms should only be used where appropriate. Minimally invasive therapies refer to all therapeutic procedures that are less invasive than open, conventional surgery. All percutaneous procedures are therefore minimally invasive; however, not all minimally invasive therapies are performed or applied percutaneously. Indeed, the term "minimally invasive" is often used by surgeons to refer to procedures performed with mini-laparotomy or with laparoscopy. Although less invasive than open surgery, these are clearly more invasive than percutaneous image-guided tumor ablation procedures. Including the term "percutaneous" as a prefix to "image-guided tumor ablations" is often too limiting, as it does not reflect the fact that tumor ablation procedures can also be performed laparoscopically, endoscopically, or surgically (13,14).

Individual procedures and therapies have often received multiple different names by various investigators, which can potentially lead to confusion. Hence, we propose and recommend a unified approach to the terminology regarding these therapies. The primary aim of this classification is to provide simplicity and clarity, most notably by eliminating extraneous detail and many acronyms. We acknowledge that some acronyms (such as RF and RFA for radiofrequency ablation and HIFU for high-intensity focused ultrasound) have gained widespread international acceptance. Nevertheless, the creation of additional niche acronyms for individual techniques should be avoided.

When discrimination between the ablation of malignant versus nonmalignant tissue is needed, the descriptive term "ablation" should still be used, with the type of ablated tissue stated afterwards (eg, acetic acid ablation of hepatocellular carcinoma, or radiofrequency ablation of angiomyolipoma, etc) In other words, the term "thermal (or laser, microwave, etc) ablation" should be used regardless of what is being ablated.

Our original document divided the different methods of tumor ablation in use at the time into two large classifications (chemical and thermal) to establish a basis for comparing modalities that differed in their specific mechanism of action but were broadly similar in application methodology or mechanism of tissue injury (1). For example, both ethanol and acetic acid instillation were considered "chemical ablation" and radiofrequency and microwave-based ablation were considered "thermal ablation." However, we now recognize that, while the utility of our classification system remains, tumor ablation has expanded to include modalities that are not completely suited to the original classification. A key case in point is the interval development of IRE as an ablative modality, as IRE is energy based with a mechanism of cellular injury that is largely nonthermal, but clearly not chemical (15). Accordingly, it is now most appropriate to divide ablative modalities into: *(a)* **chemical ablation** (ie, nonenergy ablation) or *(b)* **energy-based ablation** (ie, thermal and nonthermal). We recognize that there will be some potential crossover, as several modalities may have more than one type of mechanism of tissue injury (16). Thus, when necessary, ablation modalities should be assigned a category/classification based on the dominant mode of injury. For example, several studies have used direct injection of two or more chemicals to achieve a localized high-temperature thermal reaction to induce tissue injury—this would be considered a "thermal ablation" based on the mechanism of tissue injury (17).

Other interventional oncologic therapeutic approaches including the percutaneous delivery of genetic material, drug delivery, radiation sensitization, low-temperature hyperthermia protocols, radioactive seeds or beads, radiation segmentectomy, and the transcatheter delivery of chemoembolization may ultimately require better definition but are beyond the scope of this current position article. Nevertheless, many of the issues discussed concerning reporting criteria may likely be equally appropriate for clinical trials with those therapies as well.

Chemical Ablation

These therapies are to be classified based on the universally accepted chemical nomenclature of the agent(s) such as ethanol, acetic acid, et cetera, that induce coagulation necrosis and cause tumor ablation (18,19). For example, the term **ethanol ablation** should replace "PEI" (percutaneous ethanol instillation or injection), "PAI" (percutaneous alcohol instillation), and others (18,19). The Materials and Methods section of the manuscript should specify the route (intravenous, intraarterial, or interstitial), method of substance preparation when not commercially available or when combining agents, substances and amounts injected, delivery vehicle (size and type of needle or catheter), and rate of delivery (rapid injection or a defined rate of infusion). The intended effect should be reported, if different from complete tissue destruction (such as using ablation to enhance drug delivery, radiation sensitization, in combination with other ablation modalities). The term "instillation" for the direct delivery of pharmacologic agents is preferred given that many pharmaceuticals can be injected (a process that implies rapid percutaneous delivery) or delivered intravascularly with a catheter. This category also includes newer chemical-based therapies that have variable mechanisms of actions (such as inducing thermal injury through the concomitant injection of acid and base solutions) (17).

Energy-based Ablation

This category includes modalities that destroy a tumor either through thermal (heat or cold) or nonthermal mechanisms. For thermal therapies, energy is "applied." The term "irradiation of energy," particularly in regard to microwave ablation, is a misnomer and should therefore be avoided. The

following energy-based modalities have been described.

RF ablation.—This term (6,7,20) applies to coagulation induction from all electromagnetic energy sources within the RF spectrum (3 KHz to 300 GHz), including available "radiofrequency" and "microwave" devices (10,21). However, currently available devices traditionally designated for "radiofrequency ablation" function in the 375–500-KHz range. The term **radiofrequency** should be written as a single nonhyphenated word. Most devices currently used are monopolar in that there is a single "active" or "interstitial" electrode, with current dissipated at one or more return grounding pads. Bipolar devices have two "active" electrode applicators, usually placed in close proximity to achieve contiguous coagulation between the two electrodes (either needlelike or multitined), or on a single electrode (22). Since less common, in clinical practice today, bipolar RF ablation should be specified as such.

Microwave ablation.—By convention, the term "microwave ablation" (3,23) has been used for electromagnetic methods for inducing tumor destruction using devices with frequencies from 300 MHz to 300 GHz (21). Therefore, technically, microwave ablation devices also function within the RF spectrum and are therefore a subset of RF ablation. However, due to a different mechanism of heating and practical device and applicator differences compared with RF ablation (and described in more detail below), this category should be reported separately. Currently available microwave ablation devices function at the 915-MHz or 2.45-GHz frequencies designated for industrial, scientific, and medical (ISM) use. The term "microwave ablation" should replace the less succinct terminology of "percutaneous microwave coagulation therapy" or "microwave coagulation therapy."

Ultrasound ablation.—There are currently two methods (2,24) for the application of ultrasound energy—extracorporeal (or transcutaneous) (25) and direct (or interstitial) for percutaneous application with a needlelike applicator and for intracavitary (and intracardiac) devices (26). Hence, additional nomenclature is required to distinguish between these two groups. For transcutaneous ultrasound ablation (which does not require placement of an applicator within the target tissue), **high intensity focused ultrasound** is the preferred term, as this denotes that more than one ultrasound beam is "focused" to create an ablation. Additionally, **extracorporeal focused** ablation can also be used. Both of these terms are separate from the direct application of ultrasound energy through an applicator placed within the target tissue, which should be referred to as **interstitial ultrasound ablation**. We feel that this revised nomenclature provides a more concise and clear description of different methodologies being studied and more closely aligns several classifications being used in the literature (25,26).

Laser ablation.—The term **laser ablation** (27,28) should replace terminology such as "laser interstitial tumor therapy" (or LITT), "laser coagulation therapy," and "laser interstitial photocoagulation." This term should be used for all types of ablation using light energy. Given multiple laser technologies and application methods, including superficial therapy (contact/noncontact mode) or transcutaneous ablation, the term "interstitial" or "direct" can be reported to clarify that laser energy is applied with fibers directly inserted into the tissue.

Cryoablation.—This term (27–30) should be exclusively used for all methods of destroying tissue by the application of freezing temperatures, or alternating freezing and thawing or slight heating (31). The phrase "cryo" as a freestanding term is to be avoided, as "cryo" is a prefix and not a word. The more antiquated terms "cryotherapy" or "cryosurgery" are also to be avoided as imprecise given the introduction of newer applicators that can be introduced percutaneously, endocavitarily, or endovascularly in a minimally invasive fashion.

Rapid tissue freezing and thawing produce the greatest cytotoxic effects by disrupting cellular membranes and inducing cell death (31). In the past, liquid nitrogen was placed directly on tissue, but with a few exceptions, this method is no longer used. In the neck, chest, abdomen/pelvis, and extremities, cryoablation is generally performed using one or more closed cryoprobe(s) that are placed in close proximity to or inside of the target tumor. The most common clinically available cryoablation systems utilize the Joule-Thomson effect, which relies on the expansion of a cryogen (argon gas or liquid nitrogen) at the cryoprobe tip to cause internal temperature fluctuation. Other cooling mechanisms have also been described, but all rely on a heat sink inside of the cryoprobe and thermal conduction through the probe wall from the tissue. For publication purposes, the type of cryoablation system, the gases used, probe dimensions including tip length and total length and number of freeze-thaw cycles (active or passive thawing) should also be specified.

Irreversible electroporation.—This term (IRE or IRE ablation) (4,16) should be used for those technologies and devices that cause cell death through the repeated application of short-duration high-voltage electrical pulses that create "irreversible" injuries to cellular membranes (15). While there may be some hyperthermic ablative changes with higher-power applications, the mechanism of cell death with IRE is thought to be predominantly nonthermal (16). When describing IRE applications, relevant energy parameters that have been shown to affect outcome (including the number and length of pulses, their spacing in time, current applied, and voltage) must be adequately described (32).

Ablation Parameters

In the original version of this document, ablation parameters, such as the number of applicators and the algorithms for energy application had largely been described and developed for RF-based devices, and were described as such in a single general category. Now, there are a wide range of applicator types, device modifications,

and application techniques for several modalities, and these parameters should be clearly delineated in any reporting, so as to ensure the reproducibility of any ablation technique. We now discuss reporting terminology for applicators, application parameters, and tissue characteristics separately, and highlight modality-specific topics as needed.

Applicators

General applicator descriptions.—Although the devices are often referred to as "needles" or other nonspecific terms, they do not always conform to these precise classifications. Hence, the term **applicator** should be used when generally describing energy-based devices. Similarly, while generic needles are often used to inject agents for chemical ablation, if a device designed specifically for injection of chemical ablation agents is used, this should also be referred to as an "applicator" (33). For precision, RF and IRE applicators are **electrodes**, microwave applicators are **antennas** (rather than "antennae"), and laser applicators are **fibers**. By convention and consensus, **cryoprobes** are used to freeze tissue during cryoablation. For reporting completeness, a reference describing the appropriate applicator(s) should be cited if available; otherwise, an appropriate figure and/or schematic should be provided. A description of the applicator should also include length, a description of the active component (eg, for a needlelike RF applicator, this might include a "2-cm active tip"), and gauge size (eg, 17 gauge) (34). Gauge is preferred, as this is the common nomenclature for needle equipment used in percutaneous procedures.

Modality-specific applicator descriptions.— A description of pertinent applicator characteristics relevant to a specific ablation modality is required. For RF ablation, the geometry of the electrode (eg, active tip length) should be provided (34). For microwave ablation, the energy frequency and a basic antenna design description (eg, dipole, slot, etc) is necessary to understand energy deposition around the antenna (21). For laser ablation, in addition to the laser source (Nd:YAG, erbium, holmium, etc) and precise wavelength, additional device characteristics must be specified, including the following: *(a)* type of laser fiber (flexible/glass dome); *(b)* modifications to the tip (ie, flexible diffusor tip, or scattering dome) with dimensions and materials specified; and *(c)* length of applicator and diameter of the optic fiber (35). For IRE, active tip length, number of electrodes in the array, and interelectrode spacing should be specified (32). For cryoablation, probe caliber, gases used, applicator length, and number of probes used should be specified.

Multitined expandable applicators, cluster electrodes, and multielement antennas.—This standard terminology refers to a family of applicators that are currently available from several manufacturers for RF platforms (36) but have also been developed or are in development for chemical ablation (33) and microwave platforms (37), respectively. For RF ablation, the usual embodiment of this type of device is that of an array of multiple electrode tines that expand from a single centrally positioned larger needle cannula (36). These have been previously referred to as umbrella electrodes, multitined electrodes, Christmas tree electrodes, multiple hooked electrodes, or arrays, but this has led to confusion. Given the number of electrode types that have become available and the fact that several multitined devices are now available with variable deployment lengths, the exact electrode model and diameter of electrode array used must be specified. Also, if a stepped deployment with incremental extension of the tines was performed with a multitined device, this too needs to be explained in detail regarding the length and time of deployment. One RF ablation device uses an applicator with three parallel electrodes closely spaced together that are separately introduced into the body but have a common hub (38). This should be referred to as a "cluster electrode" [not "clustered"] and is most appropriate to describe internally cooled electrode devices in which three or more closely spaced (<1 cm) electrodes are used simultaneously to approximate a larger-diameter electrode (38). Many refer to these electrodes as "an array," which may not adequately reflect the true underlying mechanism for enhanced energy deposition and ablation.

Internally cooled applicators and perfusion electrodes.—Some devices use a cooling agent (such as saline, water, or gas) that flows within internal lumina and does not come in direct contact with patient tissues (38–40). These should be referred to as "internally cooled applicators," and should not be confused with perfusion electrodes. When internal cooling is used, specific parameters (cooling agent used, approximate temperature of the agent, perfusate volume, and rate of infusion) should be provided where applicable. Cooled applicators should also describe whether the perfusion was performed in a closed system (with no communication with the tissue) or an open system (with free infusion into tissue) (40). Perfusion electrodes have been described for RF ablation and have small apertures at the active tip or along the distal shaft allowing fluids (ie, normal or hypertonic saline) to be infused or injected into the tissue before, during, or after the ablation procedure should be referred to as perfusion electrodes. The term replaces descriptions such as "cool-wet," "wet," or "saline-enhanced" electrodes, which should be avoided.

Multipolar ablations.—Most RF ablation devices are "monopolar," applying energy through one active tip with the current dissipated on a return grounding pad. Several ablation technologies (such as multipolar RF ablation or IRE) use energy application between two or more applicators to create a zone of ablation between applicators (10,22). For multipolar applications, the number of applicators, length of active tip, spacing between applicators, and application algorithms (such as the order of energy application between different applicators) should be described (22,32).

Device and Application Parameters

Energy application parameters and algorithm of energy deposition.—For all

energy-based ablation systems, energy application parameters should be provided, including power (in appropriate terminology for the specific energy source) and duration of application. As the methods used for applying energy have undergone continuous modification and improvement, this has led to substantial confusion and difficulty comparing the results of studies performed by different groups of investigators. When reporting results, pulsing techniques and other methods for amplifying energy deposition should be succinctly elaborated on in the Materials and Methods (41). Whenever possible, a reference for the precise algorithm used (eg, ramped energy deposition or impedance regulated) and the model number of the generator should be cited. Additionally, other parameters including the use of monopolar or bipolar systems, the amount of energy applied (current and/or watts), and the total or incremental duration of ablation should be provided.

For microwave ablation, sufficient parameters must be given to at least estimate the total energy delivered. The cables that transfer power from the generator to the antenna, and within the antenna apparatus itself, are lossy and can absorb a substantial fraction of the generated power (over 50% in some systems) (21). Therefore, an estimate of the actual power delivered to the tissue should be included when describing microwave ablation results.

Multiple applicator insertions of a single applicator.—When multiple overlapping ablations are performed to achieve a single large ablation zone or an ablation zone of specific configuration, the number of ablations, mean ablation times, and the end point used (ie, imaging end point, or predetermined number of ablations) should be reported (42). If a complex composite ablation is performed, details regarding spacing and degree of overlap should be described in a manner that allows reproducibility (with many advocating for a schematic as well) (43,44).

Multiple separate applicators inserted simultaneously.—If several applicators are inserted simultaneously for simultaneous application of power (45), multipolar ablations (described above), or simultaneous ablations using "switching" technology (in which energy is applied to a single applicator at any given time, but energy application rapidly alternates between two or more applicators) (46), then specific application algorithms, ablation times, and applicator spacing should also be reported. Similarly, for multiple microwave antenna arrays, the approximate phase between electromagnetic waves applied to each antenna (if known and controlled, or acknowledged if not controlled), total power and time applied to each antenna, and pulsing parameters (if used), should also be described (47). Similar descriptions should be provided for equivalent platforms for cryoablation, and for newer ablative modalities such as ultrasound ablation or IRE (32).

Tissue Properties

Tissue-specific properties have been shown to affect the success of ablative technologies in achieving adequate tumor destruction. Characteristics of the primary organ (ie, lung, bone, liver, etc) and the tumor type (ie, hypervascular hepatocellular carcinoma vs hypovascular liver metastasis) both influence the extent of tissue injury (48). Additionally, variability in tissue characteristics in the same organ may occur based on ablation location (ie, RF ablation may be limited near the main portal vein compared with a small peripheral branch). Finally, specific ablation modalities will be affected more by one tissue characteristic than another (48,49). In general and for publication, tissue type and the effect of tissue properties on ablation (eg, proximity to adjacent blood vessels when this might impact study end point) should be acknowledged and discussed whenever relevant. Terminology specific to certain tissue characteristics has been previously described and is addressed herein.

Blood flow and airflow.—Blood flow can negatively counteract the intended modulation of tissue temperatures during thermal ablation by cooling heated tissues or warming cooled tissues (50). Similar effects have been observed from airflow in ventilated lung during pulmonary ablation (51). The term **heat sink effect** refers to the buffering effect of patent blood vessels or ventilated bronchi adjacent to the ablation zone (50,51). The shape of the thermal zone of ablation is altered away from the vessel, and the overall ablation size is diminished (50). Although this phenomenon serves to protect blood vessels and prevent bleeding from large vessels, it is also a major source of incomplete tumor ablation in many studies involving thermal ablation (52). **Perfusion mediated tissue cooling (or heating)** is a more encompassing term that refers to both the effects of the larger heat sinking vessels, as well as the substantial effects of capillary level microperfusion (53). Several strategies have been developed to overcome this problem, ranging from pharmacologically decreasing blood flow, to temporary vascular balloon occlusion of a specific vessel during ablation (ie, hepatic artery, hepatic vein, and/or portal vein during intrahepatic ablation), to intraarterial embolization and chemoembolization, to performing a Pringle maneuver (ie, temporary hepatic arterial and portal venous occlusion by direct compression of the vessels) while performing RF or cryoablation at laparotomy (10). Finally, it is further acknowledged that other fluids can be used to alter or retard uniform heating and thereby protect critical structures (such as chilled perfusate in the ureter) (54). The fluid instillation method should be adequately reported whenever employed.

Other properties.—Other tissue properties that influence tissue and tumor heating during thermal ablation include thermal conductivity, electrical conductivity (for RF ablation and IRE), tissue elasticity or fibrosis, and tissue water content and permittivity (microwave ablation). These should be acknowledged and discussed on an ablative modality and an organ/tumor-specific basis. Authors should also set out to describe the tissue homogeneity of the target tumors or stratify/quantify

those with substantial cystic components, calcification, metallic structures, graft material (eg, diaphragm or thoracoabdominal mesh), suture lines, stents (eg, ureteral or biliary) or appreciable (> 1 mm) tumoral vessels.

Ablation Procedure

Procedure Terms

As was outlined in our original standards, we continue to recommend using the term **procedure** rather than "operation," as the latter implies open surgery. We consider the term **session** to be synonymous with **procedure**. A procedure refers to a single intervention event that consists of one or more ablations performed on one or more tumors. We acknowledge that multiple ablations may be performed, either in the same procedure or as separate serial events, but as part of an overall treatment plan. The term **course of treatment** (akin to terminology currently used in radiation therapy) is now recommended to be used to describe this series of ablations. Whenever possible, this "course of treatment" should be intention based, within a well-defined time frame, and with a clearly defined end point described. The number of planned sessions and key deviations from the original course of treatment should also be explained. We acknowledge that a course of treatment may include planned treatments other than tumor ablation (eg, performing embolization prior to ablation). Thus, specific details regarding additional nonablative treatments should also be provided.

Indications

Clinical indications for tumor ablation are divided into ablations performed for **curative** intent (ie, achieving the goal of complete eradication of all known tumor cells within the index tumor[s], and without any other known tumor foci in the body) or **palliative** intent (ie, complete ablation of the index tumor[s] [6,7,19] with other known nontarget tumor foci within the body or complete or partial ablation to treat sufficient portions of the index tumor to achieve symptom relief) (29). As one cannot "palliate" asymptomatic tumors, the term **debulking** should be used when describing a procedure performed with the sole intent of reducing tumor burden or controlling disease progression.

Additionally, the specified well-defined rationale for palliative therapy and an appropriate method for assessing outcomes must be provided (ie, the intended partial ablation of given tumor). For example, when tumor ablation is used as a vehicle for pain reduction (such as pain from osseous metastases), pre- and postprocedure pain scales and medication use (using commonly used scales such as morphine equivalent dose) should be obtained (55,56). If ablation is employed to reduce symptoms of a syndrome (such as carcinoid or other hormonally active or paraneoplastic tumors), appropriate documentation of laboratory results from blood or urine before and after therapy must be provided, and other symptomatic end points and grading systems must be specified and employed. Standardized questionnaires should also be used for quality of life assessment when appropriate (55).

Complete ablation of symptomatic benign tumors (such as osteoid osteomas, tender breast fibroadenomas, or hormonally active benign adrenal aldosteronomas) to complete symptomatic relief can also be considered curative (57–59).

Adjuvant Therapies

In the original standards document, "adjuvant therapies" referred to those therapies administered concomitantly with or during ablation to potentiate local effects of ablation. For example, the percutaneous instillation of sodium chloride solutions was used to alter electrical and thermal conductivity during RF ablation. Increasingly though, tumor ablation is now being combined with a multitude of agents, ranging from those given to potentiate the local antitumor effects of ablation, to the concurrent or staged administration of systemic chemotherapy while simultaneously performing local ablation (7,60). **As such, the original general description of "adjuvant therapies" is felt to be sufficiently nonspecific and archaic**. The more precise following descriptions should replace this term.

Concomitant agents.—This includes those agents that are being used to potentiate the local effects of tumor ablation (without having a specific independent antitumoral effect). For example, sodium chloride fluid or iron oxide particles injected into the target tumor prior to RF ablation have been described. Hence, specific details of the agent used (ie, agent/substance/liquid concentration, route and rate of administration, timing in relation to the ablation) must be provided. Whenever possible a reference for the precise algorithm and the rationale for the selected concomitant agent should be provided. An additional term, "sensitizers," is used to describe certain treatment-enhancing agents in radiation therapy, and may be appropriate here as well (61).

Combination therapies.—This includes cytotoxic or chemotherapeutic agents that, while having known independent antitumor effects, are administered in conjunction with (and temporally close to) ablation with the specific intent of inducing a synergistic effect (eg, RF ablation combined with transarterial chemoembolization [or TACE], antiangiogenic agents such as sorafenib, liposomal doxorubicin, or ethanol) (8,60). Specific details of the agents used should be provided, along with a rationale for their use (whenever possible).

Concurrent therapies.—This includes agents that have known antitumor effects that are administered at the time (or around) of ablation, but either have not been shown to interact with ablation, or are without clear mechanisms of synergy, or are administered without intent to potentiate effects of one or the other therapy (eg, systemic chemotherapy or radiation therapy, or cementoplasty after bone ablation) (7,62). Specific administration timing related to ablation (and any predetermined periods of cessation around ablation) should still be described, as these therapies may ultimately be proven to effect end-point outcomes.

We also acknowledge that with greater understanding of potential systemic effects of local ablation, agents may be combined with tumor ablation to modulate secondary systemic effects (without intended effect on local tumor ablation efficacy). Examples of this include modulating antitumor immunity after tumor ablation using vaccines or immunomodulatory agents (63). Yet, this area of research is too premature to provide a well-defined classification system. Regardless, in all circumstances, specific details of administration, rationale, and use should be provided. For example, in clinical studies in patients treated with ablation, details regarding prior or concurrent systemic chemotherapy treatment (first- and second-line regimens) should be provided.

Image Guidance

While all procedures referred to in this communication refer to tumor ablations guided by imaging, it is important to understand what is meant by the term "image guidance." First, *guidance* refers to procedures in which imaging techniques (eg, fluoroscopy, US, CT, PET, and MR imaging) are used during the procedure. Imaging is used in five separate and distinct ways: planning, targeting, monitoring, intraprocedural modification, and assessing treatment response (64). Different imaging techniques can be used, alone or in combination, to successfully perform each of the procedural steps described. While CT and MR imaging use have been traditionally described, contrast material–enhanced US is also now well established and commonly used in performing image guidance for all parts of an ablation procedure, and in many different organs (65). Treatments are planned before the procedure, and the assessment of treatment response occurs after the procedure is completed. Targeting, monitoring, and intraprocedural modification are all performed during the procedure. The meaning of these terms is described further as follows.

Planning.—Imaging techniques, including US, CT, MR imaging, and more recently PET/CT, are used to help determine whether patients are suitable candidates for these procedures. Imaging aspects that are particularly important include tumor size and shape, number, and location within the organ relative to blood vessels, as well as critical structures that might be at risk for injury during an ablative procedure (66). Additionally, disease-specific cancer staging (which may include additional imaging of nontarget areas) should also be provided. Adopting similar terms to radiation therapy is acceptable, such as "planned treatment volume" (or PTV).

Targeting.—This term is used to describe the step during an ablation procedure that involves placement of an applicator (eg, an RF electrode or cryoprobe) into the tumor. While much of the current image-guided tumor ablation literature describes the use of techniques such as contrast-enhanced US and CT to target tumors for purposes of ablating them, targeting is only one aspect of intraprocedural image guidance. Ideal qualities of a targeting technique include clear delineation of the tumor(s) and the surrounding anatomy, coupled with real-time imaging, and multiplanar and interactive capabilities. For example, US (66) and some MR imaging systems (67) have all of these qualities.

Image-fusion and navigation systems that combine multiple modalities (such as US and MR imaging with CT) have also been developed and are used with ever increasing frequency for tumor targeting (68,69). These devices should be appropriately described, including the type of source/reference images and real-time images incorporated into the fusion and projections displayed. Methods of registration should be described (ie, rigid vs elastic, fiducial-based vs landmark selection, software source, and level of automation clarified where appropriate). Errors should be described in terms of overall accuracy (system error), registration error (root mean square error where applicable), and target to registration error (or TRE) (68,69).

Monitoring.—Monitoring is the term that is used to describe the process by which therapy effects are viewed during a procedure. Changes in imaging that occur during a procedure can and should be used to determine treatment effects. For example, the zone of cryoablation can be effectively monitored with US, CT, and MR imaging by virtue of appreciable changes in tissue reflectivity, density, and phase as tissues solidify with freezing, respectively. Important aspects of monitoring include how well the tumor/target is being covered (ie, included and/or encompassed) by the ablation zone, and whether any adjacent normal structures are being affected at the same time. Not all image-guidance techniques provide the same degree and types of monitoring. For example, MR imaging is currently the only modality with well-validated techniques for near real-time temperature monitoring. For thermal monitoring, temperature measurements within the applicator and/or the ablation zone, when reported, should include specification as to where the temperature was measured (ie, where the temperature sensor is located in the applicator, or if a separate thermocouple was used), and when during the ablation temperature measurements were acquired. For noninvasive thermal monitoring (ie, with MR imaging), additional descriptions of how this was performed (eg, number of sections and imaging plane), and specific imaging sequences used, should be provided. If other forms of monitoring are used, such as measuring evoked potentials during ablation near nerves or of intramuscular tumors, then detailed descriptions should be provided. The term "monitoring" should not be used to describe response to treatment; for this, "treatment assessment" or "follow-up" is used.

Intraprocedural modification.—This term was previously referred to as "controlling" and is used to describe the intraprocedural tools and techniques that are used to perform "real-time" modification of the ablation treatment. In order to control an image-guided ablation procedure, the treatment should be monitorable, such that the operator can utilize the image-based information obtained during monitoring to modify

the ablation treatment as needed to control it. This may simply be repositioning of a therapy applicator based on physician experience, imaging findings, and thermal feedback, or it could be as sophisticated as an automated system that automatically terminates the ablation at a critical point in the procedure. This also includes intraprocedural imaging with cone-beam CT or CT, PET, MR imaging, or US, when used for assessment of effect or repositioning.

Assessment of immediate treatment response.—Imaging used to immediately assess an image-guided tumor ablation procedure occurs after the procedure is completed (10–12). Immediate assessment after ablation procedure should demonstrate that the target end point has been reached. When ablation is performed with curative intent, assessment should demonstrate that the ablation zone encompasses the target tumor including a circumferential ablative margin (at least 5 mm, and ideally 10 mm all around the tumor) (70). Use of a contrast agent during procedures should be well described, including agent volume and timing of imaging.

Ancillary procedures.—As one of the main considerations in thermal ablative strategies has been nontarget injury to nearby structures, several techniques have been described to separate critical nontarget structures from the target ablation zone (54). One key technique involves injection of fluid using a separately introduced hollow-bore needle to create separation, and was initially termed "hydrodissection." This concept has now expanded to include the injection of air, creation of artificial ascites or pneumothorax, and mechanical displacement using balloon catheters. Additionally, mixing injected fluid with an iodinated contrast agent to improve visibility has also been described. When these techniques are used, a description of the injected agent (such as saline or sterile water, with or without contrast agent), the technique used to introduce the agent (such as needle caliber and length), and the end point (such as specific distance between structures or a set volume of the agent), should also be included. Likewise, denoting the agent used with the prefix **hydro-** or **pneumo-** combined with dissection is also recommended. **Displacement** is the appropriate term to describe separation of the target from the nontarget structure.

The use of saline and/or externally applied warming or cooling bags for overlying skin protection are additional examples of ancillary procedures. Use of thermal balloons to control/protect surrounding tissue temperatures should also be noted, such as for ablations near ureters, the urethra and/or esophagus. Similarly, intraluminal perfusion to protect nontarget structures, such as for renal pelvicalyceal, ureteral, and bile duct protection, should also be specified, when used.

Pathologic and Imaging Findings

The difference between pathologic findings and imaging findings must be stressed by the appropriate selection of terminology. Although in many cases there is a good correlation or overlap between radiologic and pathologic findings, this is not invariably the case, as over- and underreporting of the true extent of disease has occurred (12,71). The classic example of this is assuming that imaging findings (ie, the zone of abnormality on the image) are equivalent to the pathologic findings (ie, the true zone of tumor destruction/treatment effect), which may not be the case. Hence, careful differentiation between imaging findings and pathologic findings must be made. This distinction is critical given that our accuracy at assessing the extent of tumor destruction by using imaging is limited by the resolution of imaging and uncertainty about the viability of cells within the radiographic margins of the zone of ablation (72).

Zone of Cell Death at Pathologic Examination

As newer technologies such as IRE induce tissue injury through nonthermal mechanisms, thus the term **treatment effect** should be used globally to describe the gross pathologic changes from ablation. For thermal ablation, the gross pathologic appearance of treated tissue should continue to be referred to as **coagulation** (which is associated with those pathologic findings associated with high-temperature thermal injury). Given that many tumors undergo central necrosis without ablation therapy, the term "coagulation" is preferred over the use of "necrosis," as it denotes that the ablation intervention is actively leading to tumor destruction. The more generalized term "coagulation" is preferred over the term "coagulative necrosis," as the latter term has a well-defined meaning within the pathology literature including absence of visible nuclei within the dead cells. In actuality, the zone of coagulation, while predominantly comprised of coagulative necrosis, often lacks the classic, well-defined histologic appearance of coagulative necrosis in the acute postablation period or even within some zones of adequately ablated tissue for many months following ablation (73). Additionally, for thermal ablation, short-duration high-temperature exposure results in a well-known "thermal fixation" effect, which preserves cellular architecture despite cell death, making interpretation of pathologic findings based on traditional features of "coagulation necrosis" difficult (74). When histopathologic evaluation of the ablation zone is performed, tumor cells identified in morphologic stains (hematoxylin-eosin) should undergo additional evaluation with specialized immunohistochemical stains to determine viability or irreversible cell death (72,75). Both histopathologic and immunohistochemical evaluation of the ablation zone are recommended for articles reporting on pathologic findings or performing radiologic-pathologic correlation after tumor ablation (73). The term "coagulation" should also be used to describe pathologic findings caused by newer ablation technologies, such as microwave ablation and IRE, as well.

Another important issue is defining the zone of ablation at gross pathologic examination. Most thermal therapies induce a central "white zone" of coagulation, a pathologic finding that is generally accepted to represent

coagulated tissue, surrounded by a variable "red zone" of hyperemia, which is most often absent in *ex vivo* specimens (76). However, there has been controversy in measuring and hence comparing the "true" size of induced zones of ablation based on the fact that some have reported that this more peripheral "red" zone also represents ablated tissue and include it in their measurements. To avoid confusion, both measurements (the zone of complete ablation alone and the extent of the inflammatory zone) should be provided. Furthermore, these descriptions apply closely to thermal ablation, but may not be as applicable to other modalities such as IRE or chemical ablation (77). Therefore, terminology such as "central ablation" and "peripheral inflammation" can also be used. This should be differentiated from the thickness of the ablation transition zone, which describes how much spatial zone resides between devascularized and dead tissue and normal/unaffected tissue. This has been called the "hyperemic rim" or "benign periablational enhancement" (at imaging), but could be described simply as the "transition zone." At a minimum, the zones included in gross pathologic measurement should be specified. Where appropriate, for newer technologies, histopathologic results with viability staining should be correlated to gross pathologic changes.

Zone of Ablation at Postprocedural Imaging

Appropriate terminology must reflect the fact that although we rely on imaging to define the gross extent of induced coagulation, our accuracy is limited by both spatial and contrast resolution to approximately 2–3 mm depending on the imaging modality employed (73). Hence, postprocedural imaging findings are only a rough guide to the success of ablation therapy because microscopic foci of residual disease cannot be expected to be identified with standard imaging. The term "ablation zone" can be used to describe the radiologic region or zone of induced treatment effect (ie, the area of gross tumor destruction visualized by using imaging). The term "lesion" is to be avoided given potential confusion as to the intended meaning, as the term "lesion" has been used to refer to both the "ablation zone," as well as the underlying tumor to be ablated itself. Reporting of the ablation zone should be made in relation to the target tumor. In order for the ablation to be considered successful, the target tumor should be completely covered by the ablation zone that includes at least a 5–10-mm margin all around the expected tumor margin (70).

There are two types of imaging findings that are identified following an ablation procedure, those related to zones of decreased perfusion (73) and those in which the signal intensity (at MR imaging), echogenicity (at US), attenuation (at CT), or tracer uptake (at PET) are altered (78). Hence, the imaging strategy employed and the criteria used to define ablation must be specified. Timing of early or "immediate" imaging should be described when performed. For contrast-enhanced studies, it is important to recognize that in some organ sites, and in particular the kidney, minimal contrast enhancement (ie, for CT, < 20 HU) early after ablation can be identified in areas that are subsequently proven at pathologic examination to be uniformly dead tissue (79). This finding is not well understood but may be due to pseudoenhancement, as has recently been described for renal cysts, or alternatively to represent true minimal enhancement from leaky capillaries at the treatment margin.

Finally, we acknowledge that imaging findings after tumor ablation differ based on ablation modality, imaging modality, tumor type, and organ site of ablation. Our original document included specific imaging features of thermal ablation of the liver, where terminology at the time was unclear or poorly defined. The field of image-guided tumor ablation has expanded sufficiently that standardization of descriptive terminology for postablation imaging findings that are modality and organ/tumor specific now falls beyond the scope of this document. Key terminology for imaging will be reviewed and reported in a separate consensus document.

Ablative Margin

For many disease processes and particularly for tumors in the liver, the ablation of appropriate margins beyond the borders of the tumor is necessary to achieve complete tumor destruction. The term "ablative margin" is used to describe the region that should ideally be ablated in these cases (1,44, 70). This term is preferable to "surgical margin," as there is no surgery. Although most investigators place this at 5–10 mm for many processes, particularly those in the liver, lung, and kidney, data are currently lacking to support definitive recommendations regarding the ideal margin size at this time (70,80). Accordingly, the extent of desired or intended ablative margin should be specifically mentioned. It is important to stress that an extensive ablative margin, while desirable in curative ablation, is not always necessary or desired when sparing of uninvolved organ parenchyma is required. For example, when attempting to destroy focal tumors in the kidney in patients having a tendency toward the development of multiple tumors such as those with von Hippel-Lindau syndrome, nephron sparing and more limited ablation are desired to preserve renal function and avoid dialysis (81).

For normally vascular organs such as the kidney and liver, creation of an ablative margin results in zones of low attenuation and absent perfusion extending into the parenchyma (78,82). Increased attenuation occurs in low-density tissues such as perinephric fat (for exophytic renal or adrenal tumors) and in the lungs where the term "ground glass opacity" is used to describe the imaging findings of the treatment zone surrounding and including the ablated lung tumor.

Involution of the Ablation Zone

The term "involution" should describe the process by which the body eliminates the zone of induced coagulation over weeks to months. The term "shrinkage" should be avoided as being

imprecise. The term "regression" is likewise to be avoided given that it is commonly used in the medical oncology literature to describe involution of just the tumor itself, rather than the induced coagulation that often involves both tumor and the surrounding tissues (ie, the ablative margin). It is important to note that the lack of or minimal involution does not imply treatment failure. This is a finding that has been described for multiple ablation modalities (eg, RF ablation, and more recently, IRE) (78). Cicatrization may accompany involution, where nearby tissue is retracted toward the treatment zone.

Reporting of Tumor and Ablation Sizes

Appropriate uniform guidelines and standards are needed for the reporting of the extent of induced coagulation. In the past, comparison between technologies has been made somewhat difficult based on the fact that some authors report the largest diameter of induced coagulation, others report the average diameter, while some report the short-axis diameter. Additionally, coagulation has occasionally been reported as a volume of ablated tissue without any definition of dimensional measurements. Finally, zones of coagulation often demonstrate nonspherical shapes, and variations in cross-sectional axis can introduce variability in ablation size measurements. Hence, uniform standards of comparison are essential and must be adopted. It is also important to acknowledge that volumetric assessment for staging is also not yet uniform or standardized in the oncology community, but will likely be increasingly important for ablation, as noted below.

A three-dimensional, or whenever possible volumetric evaluation, should be performed to measure the ablation zone (80). While software to perform volumetric quantification of the ablation zone is being developed and not in widespread clinical use, we recognize that this technology may ultimately provide a means for detailed evaluation (83). At a minimum, characterization with multiplanar imaging (which is now widely available in clinical practice) should be performed. Additionally, it is important to acknowledge variability in postablation size measurements, which can be more or less significant depending on the ablation modality. For example, microwave ablation and, to a lesser degree, RF ablation can lead to significant tissue contraction after ablation, resulting in a smaller apparent ablation zone at postprocedure imaging (84). The visible "ice ball" during cryoablation likely overestimates the size of the ablation zone, as the cytotoxic isotherm is several millimeters inside the ice-ball margin (85). Finally, a successful ablation zone will be significantly larger than the target tumor and therefore traditional Response Evaluation Criteria in Solid Tumors, or RECIST, do not address successful ablation (86). Therefore, the first postablation imaging (eg, contrast-enhanced CT or MR imaging) is the new baseline imaging for further assessment of the ablation zone and detection of subsequent local tumor progression.

Ablation index tumor.—**Ablation index tumor** is the preferred term for the initially identified tumor prior to ablation. This tumor should not be referred to as a "lesion," as this term could be confused with the zone of induced coagulation or the region of ablation at imaging. This should be distinguished from other "index tumors" defined by response criteria for prior courses of systemic chemotherapy or radiation therapy.

Size classification of tumors.—Actual tumor sizes (mean ± standard deviation, and range if applicable) should be reported. Given that the appropriate ablation of adequate margins often represents the rate-limiting step for treatment efficacy, the maximum diameter of the original tumor must be specified (based on Response Evaluation Criteria in Solid Tumors 1.1). However, many investigators perform analyses of their results based on stratification of tumor sizes. In this regard, there is often too much ambiguity and variability in the categorization of tumors by size. Different investigators have reported an upper limit of 2, 2.5, 3, and 5 cm as "small tumors" and 5 or 10 cm as large. This has made the direct comparison of results using different technologies challenging. We therefore continue to recommend that if such categorization is performed that the tumor size classification should be standardized according to the following scale: small tumors as 3 cm or smaller in diameter, 3–5-cm tumors as intermediate, and tumors larger than 5 cm as large. This classification was determined as most practical because it parallels the current technical capabilities and efficacy for most image-guided ablation therapies and has proven to be reproducible in clinical practice (7,8).

Comparing Zones of Coagulation among Different Ablation Techniques

Often the extent of induced coagulation is reported in experimental studies as a vehicle for comparing different ablation technologies and parameter modifications (87). The extent of induced coagulation should include reporting of the short-axis diameter, given that this parameter influences the overall extent of necrosis that can be achieved from a single application of energy, and is likely to be an important factor influencing technical success in clinical practice. Hence, while additional parameters can certainly be provided and may be potentially useful, at a minimum, this should be the standard that is reported to enable honest comparison between techniques. Of course, given that the ablation of a tumor is performed in three dimensions, ideally, all three-dimensional measurements of the ablation zone and tumor, and less ideally both measurements of the cross-sectional area should be provided. If volume is to be used as the only reported parameter, then a rationale must be specified. Average diameters should only be accepted if the tumor or zone of ablation is truly spherical, varying not more than 2–3 mm in cross-sectional diameter. It is further well known that many devices produce irregularly shaped zones of coagulation. Hence, the degree of uniformity or irregularity in the shape of the ablation zone should be specified. Finally, some ablation technologies, most notably microwave ablation and to a lesser extent

RF ablation, can cause relatively immediate local tissue contraction secondary to collagen and other protein remodeling, profound water evaporation, and tissue dehydration in the ablation zone (84). As a result, postablation measurements of the ablation zone at imaging or gross inspection likely underestimate the preablation tissue dimensions. Because the amount of contraction varies with ablation time, temperatures, and energy type, postablation measurements alone may not be suitable for directly comparing all technologies.

It is important to stress that reliance on minimum and maximum sizes for the zone of ablation may not be useful for predicting clinical technical efficacy, as other technical factors are likely to be equally important. For instance, depending on the orientation of the energy applicator, a 1 × 2-cm tumor may be adequately treated by using a 2 × 3-cm zone of ablation, but not by using a 3 × 2-cm zone of ablation. Ablation diameter or volume may also not tell the entire story. Although a 3-cm zone of coagulation may completely cover a 2-cm tumor when correctly positioned, if off the mark, it will fail to destroy the entire tumor.

Standardization of Follow-up

Currently, defining appropriate length of follow-up and the time points for defining technical success are not well established. One investigator's long-term follow-up is often another's short-term follow-up. Hence, specific guidelines need to be adhered to depending on the type of disease treated, and the intended goal of the study. Particularly, if existing standards for overall length of follow-up exist for a specific type of tumor, then those practice guidelines should be followed when treating those cancers with ablative therapies. Treatment study goals are generally related to one or more of the following four categories, which usually need to be distinguished from one another: *(a)* **technical success**, or was the tumor treated according to protocol?, *(b)* **technique efficacy**, or was the tumor effectively ablated? *(c)* morbidity, or were critical structures and **complications** avoided? and *(d)* **outcomes**, or was there some improvement in tumor control, patient survival, quality of life, or palliation?

Technical Success

This term simply addresses whether the tumor was treated according to protocol and was covered completely by the ablation zone. Tumor coverage can be assessed either during or immediately following the procedure, most often with contrast-enhanced CT or contrast-enhanced US. A tumor that is treated according to protocol and covered completely (ie, ablation zone completely overlaps or encompasses target tumor plus an ablative margin), as determined at the time of the procedure, is "technically successful." The importance of this term is to help investigators separate out those patients in whom the protocol could not be executed completely, either for technical reasons or for reasons related to comorbid disease, from those who were treated according to protocol. As outlined above, a predefined course of treatment may include several ablation procedures spaced out over time. Primary technical success should be determined at the first follow-up imaging study after completion of the predetermined course of treatment.

Technique Efficacy

Distinction between "technical success" and "technique efficacy" must be made for each treated tumor. Efficacy can only be demonstrated with appropriate clinical follow-up. "Technique efficacy" should therefore refer to a prospectively defined time point (ie, immediately following the last course of a defined ablation protocol, 1 week, or 1 month after treatment) at which point "complete ablation" of macroscopic tumor, as evidenced by imaging follow-up (or another specified end point), was achieved. The number of sessions (ie, the number of interventional procedures) to achieve the specified end point should likewise be defined. Authors are encouraged to report whether or not this complete ablation included an ablative margin and how this was determined (ie, what imaging modality).

Comparison of technical success and efficacy between various ablation protocols has been challenging, as many authors have adopted different terminology or guidelines. This problem is further compounded by our ability, and often the clinical need, to ablate a tumor over many sessions and the possibility of ablating growing foci of local tumor progression months after the initial course of therapy. A window of initial therapy for each ablation technique during which it is reasonably expected for the tumor to be completely ablated should be defined. For percutaneous thermal ablation, ideally this should not exceed an upper limit of either one to four procedures or a specified time frame (up to 1–3 months), depending on the size, type, and location of the tumor, as well as the rationale for therapy. We have purposefully left definition of this end point as a broad range, given evolving consensus on defining more specific parameters, as each disease process may vary. If complete ablation cannot be achieved within these specified parameters, the tumor should be classified as "unsuccessfully treated."

Primary and secondary technique efficacy rates.—Given that multiple treatments of image-guided tumor ablation therapy are often given over the course of the disease, primary and secondary technique efficacy rates should be reported. The **primary efficacy rate** is defined as the percentage of target tumors successfully eradicated following the initial procedure or a defined course of treatment. The **secondary or assisted efficacy rate** is defined as including tumors that have undergone successful repeat ablation following identification of local tumor progression. The term **retreatment** should be reserved for describing ablation of locally progressive tumor, in cases where complete ablation was initially thought to have been achieved based on imaging demonstrating "adequate" ablation of the tumor.

The technical success and technique efficacy rates are very important as we define the limitations of our technologies, ideally in a manner similar to other disciplines (ie, surgical resection articles typically report a positive

margin rate). Nevertheless, for some protocols, the concepts of local technical success and local tumor progression (ie, technique efficacy) may have limited impact on the most important outcome parameter—patient survival. For example, using three to four procedures or 1 month as the window may be of secondary importance if the patient lives for 5 years because of the treatment, or if the tumor is completely eradicated over multiple courses of ablation therapy over many years.

Disease progression.—Disease progression may be considered in three ways.

1. Residual unablated tumor versus local tumor progression. When initial follow-up imaging demonstrates residual tumor at the ablative margin, this is referred to as **residual unablated tumor**. **Local tumor progression** describes the appearance of tumor foci at the edge of the ablation zone, after at least one contrast-enhanced follow-up study has documented adequate ablation and an absence of viable tissue in the target tumor and surrounding ablation margin by using imaging criteria. This term applies regardless of when tumor foci were discovered either early or late in the course of imaging follow-up.

The term **local tumor recurrence** implies the appearance of new tumor foci at the ablative margin after local eradication of all tumor cells with ablation. However, pathologic determination of a "clear margin" cannot be made after most cases of image-guided ablation (6,7). Accordingly, the appearance of tumor at the ablative margin at imaging likely represents residual untreated microscopic tumor, and therefore, this term should be avoided.

2. Causes of disease progression. The distinction between local incomplete therapy (local tumor progression), new foci of disease within the target organ (especially the liver), and distant malignancy should be distinguished whenever possible and reported on. Discrimination between "local tumor progression" and new tumor is important for determining the potential utility (ie, local treatment success rate) of a given method, in the setting of many potentially confounding causes for the demise of a given patient. Additionally, for patients with cirrhosis, the causes of mortality should be differentiated between hepatic disease and others.

3. Complete ablation versus partial ablation. When complete ablation is not achieved, classification of the degree of partial ablation should be avoided. For example, either reporting a percentage of the tumor ablated, or using descriptions of "near complete ablation" (to refer to ablation zones that encompass 90%–95% of the tumor) should be avoided. This kind of classification of partial ablation is not warranted given that adequate data are lacking to support a difference in outcome between different levels of partial ablation. Furthermore, such percentages are often estimates and may be inaccurate. Hence, for cases with curative intent, partial ablations should either be considered technical failures or simply noted as incomplete ablations as appropriate.

Complications

Classification.—The unified standardized SIR grading system should be used as outlined (88). Complications should be reported using the most recent version of the SIR Classification standard table so that they can be categorized consistently according to severity. The definition of death is self-explanatory and should be reported on a per-patient basis. Any patient death within 30 days of image-guided tumor ablation should be addressed (SIR classification F). The specific cause of death should be reported, with the potential and degree of causality to the ablation procedure clearly specified. Major and minor complications and side effects should be reported based on the number of ablation sessions on a per-session basis. However, ideally, the number of ablations performed should be included, as multiple ablations increase the likelihood of complications.

The definition of **major complication** is an event that leads to substantial morbidity and disability (eg, results in the unexpected loss of an organ) that increases the level of care, or results in hospital admission, or substantially lengthens the hospital stay (SIR classifications C–E). This includes any case in which a blood transfusion or interventional drainage procedure is required. All other complications are considered minor. It is important to stress that several complications such as pneumothorax or tumor seeding can be either a major or minor complication depending on severity. For tumor seeding this would depend on whether or not the ectopic tumor focus can be successfully ablated or otherwise treated.

Differentiation among immediate complications (up to 6–24 hours following the procedure), periprocedural complications (within 30 days), and delayed complications (greater than 30 days after ablation) is advised. This stratification will give the reader an idea when specific complications/side effects are most likely to occur and assist in defining when and how to take adequate precautions. Ablation-related complications should include problems encountered within the periprocedural (30-day) time period that can be related in any way to the procedure, as well as additional complications that were identified at delayed follow-up imaging that were judged to be highly likely due to the ablation therapy (biliary ductal stricture, tumor seeding along the needle track, etc). Additionally, it should be specified which complications are being reported on a patient-by-patient basis (such as death) and for which the denominator represents the number of sessions, or by the number of tumors.

Alternative classifications exist, and can be used if a compelling reason is provided. For example, the Common Terminology Criteria for Adverse Events (CTCAE) v4.0 of the National Cancer Institute and the Clavien-Dindo classification system are commonly used systems in oncologic and surgical practice (89,90).

Side effects.—Side effects are expected, undesired consequences of the procedure that although occurring commonly, rarely, if ever, result in substantial morbidity. These include pain, the postablation syndrome, and asymptomatic pleural effusions and minimal asymptomatic perihepatic (or renal)

fluid or blood collections seen at imaging (78). Another such side effect would include asymptomatic imaging evidence of minimal thermal damage to adjacent structures without other evidence for negative sequelae (ie, "collateral damage"). An example of this would include when the zone of ablation extends beyond the liver capsule to include small portions of the diaphragm or kidney. These are not true complications, as they do not lead to an unexpected increased level of care.

Pain.—Even with appropriate conscious sedation techniques, patients may experience pain during ablation procedures. Additionally, depending on the organ site, many patients may experience grade 1–2 pain for several days, occasionally lasting 1–2 weeks following an ablation procedure. Last, thermal ablation, particularly RF and cryoablation, are being used with increased frequency as a method for treating refractory metastatic and primary bone tumor pain. We therefore propose adopting the Common Terminology Criteria for Adverse Events (CTCAE) v4.0 of the National Cancer Institute for the reporting of pain (90).

Postablation syndrome.—This syndrome is a transient, self-limiting symptom/sign complex of low-grade fever, nausea, vomiting, and general malaise. The duration depends on the volume of necrosis produced and the overall condition of the patient. If small areas are treated, the patient is unlikely to experience postablation syndrome at all. If very large areas of liver tumors are ablated, the syndrome may persist for 2–3 weeks. The majority of patients who get this syndrome will experience some malaise for 2–7 days, depending on the volume of tumor and surrounding tissue ablated and the integrity of the patient's immune system (ie, patients receiving steroids or with small tumors may have no postablation syndrome).

Follow-up and Outcomes

Outcomes of interest may include the following: local response (by imaging assessment), systemic response (pain, cancer syndromes, etc), quality of life, time to progression (or progression-free survival) or overall survival. For those studies that deal with quality of life, some form of objective measurement must be used both before and after treatment (91). Ideally, previously validated scales or metrics should be used and appropriately referenced.

Imaging follow-up.—Currently, despite a reliance on imaging findings to determine the extent of "unablated residual tumor," there is a lack of consensus on a standard follow-up interval regimen for imaging. The most common approach taken by members of the Working Group include contrast-enhanced imaging (US, CT, MR imaging, or PET) within 6 weeks of the initial ablation to determine whether or not additional ablation therapy is required (many centers perform this on the day of the initial procedure), and thereafter every 3–4 months, to determine technique efficacy. Imaging intervals may also vary depending on the type of underlying tumor and the goals of treatment. At a minimum, the intervals at which imaging follow-up were performed should be clearly specified. A more comprehensive, separate document describing approaches and standardization of imaging follow-up is forthcoming.

Although standard imaging criteria for response assessments have been defined for evaluation of other cancer therapies, these criteria focus almost exclusively on tumor size. Yet, exclusive reliance on tumor size does not provide a complete imaging assessment of tumor response, and may even lead to erroneous conclusions as to the efficacy of the therapy (86). Therefore, in addition to reporting index tumor diameter and the diameter of the zone of ablation, assessment of tumor enhancement or lack thereof should also be included in the imaging response assessment following ablation therapy. This approach is consistent with the incorporation of tumor enhancement as a measure of treatment response in newer imaging criteria (92).

Length of follow-up.—Compared with the original document, now much of the data from clinical studies has matured, and 5- and 10-year follow-up data are becoming available (6–8,92). In this context, some standardization of reporting clinical follow-up is required. Here, we define these end points as *(a)* technical success and early safety data should have 6-month follow-up, *(b)* preliminary clinical outcome results should have a minimum of 1-year follow-up, *(c)* intermediate-term data should have 3-year follow-up, and long-term data should have at least 5-year (and ideally longer) data, clearly specifying whether this is mean or median follow-up. Adopting this approach ensures that clinical data for ablation meet benchmarks used by other specialties. When assessing survival and disease-free survival, an appropriate length of follow-up should be selected based on tumor biology and accepted criteria for other therapies for a given tumor type. For example, surgical literature has required long-term follow-up of greater than 5 years for determining the impact of various therapies on survival for colorectal metastases to the liver or hepatocellular carcinoma (93). For other tumors, the appropriate length of follow-up may vary, and indeed for more rapidly growing tumors such as in the lung, the length of follow-up may be shorter. For slow-growing tumors, such as low-grade primary renal cell carcinoma, the length of follow-up may need to be longer (6).

Clinical outcomes.—For all studies reporting intermediate or long-term ablation outcomes, metrics of **overall survival (OS)** should be reported (including percentage survival at specified time points, and mean and median survival times). OS should be calculated from the start of ablation treatment rather than treatment completion. Additionally, OS should also be reported from the date of cancer diagnosis. The time interval between treatment initiation and disease progression, **time to tumor progression (TTP)** (and its associated metric, **progression-free survival [PFS]**) is also increasingly used as a measure of how effective tumor ablation is in achieving local tumor control, particularly in patients receiving more than one treatment where interpreting the effect of ablation on OS can be difficult. "Local TTP or PFS" (reflecting the

incidence of progression in the ablated index tumor[s]) should be differentiated from "organ-specific TTP or PFS" (representing tumor progression or lack thereof in the diseased organ, such as liver), and both reported. For "tumor-related" death, determination of local TTP or PFS (eg, differentiating death due to local tumor progression or diffuse metastatic burden) will often be useful, as it can potentially shed further light on the efficacy of local therapy. As for OS, PFS should be calculated from the time of treatment initiation. Definitions of "progression" should also be provided (eg, percentage increase in tumor size), and any imaging response assessment criteria used should be specified. Where tumor ablation is performed for symptom relief, **symptom-free survival** may be a more appropriate descriptor. For some oncologic populations (such as early-stage renal cell cancers or small hepatocellular cancers), substantial non–cancer-related patient mortality (unrelated to or even masking ablation efficacy) may be anticipated, particularly in clinical studies with long-term follow-up. In this case, the cause of death should be specified as related or unrelated to the patient's underlying malignancy (**cancer-specific survival**). Finally, risk adjustors should be reported as appropriate for the organ/disease involved (eg, performance status using Eastern Cooperative Oncology Group or Karnofsky scores).

Other Important Aspects Requiring Attention When Reporting Clinical Results

Technique Parameters to Be Provided for Publication

It is our belief that many published series do not provide enough technical detail to permit duplication of the investigators' efforts. This problem is compounded by the fact that there are many different types of ablation equipment on the market and in development, and these often change. Hence, the specification of the parameters such as duration of application energy applied, manufacturer, et cetera, must be provided. Particularly, in clinical trials where several different devices and techniques are used, a clear description of device and applicator selection, and determination of ablation end point should be provided. A clear table that details how often specific devices and techniques used should also be provided. Also, the number of treatment sessions for each tumor should be specified. The procedure approach (ie, whether the procedure was performed percutaneously, laparoscopically, or endoscopically) should also be clearly specified. Additional parameters to be provided for publication should include the following: *(a)* whether the procedure is performed under general anesthesia or conscious sedation (the specifics of anesthesia and medications administered during the procedure and in the recovery phase should always be reported, including agent, dose, route, etc), *(b)* the types of imaging guidance (CT, CT fluoroscopy, US, PET, and/or MR imaging), *(c)* whether or not the patient was hospitalized, *(d)* the number of sessions required to initially achieve technical success, and *(e)* the subsequent rates of other tumors requiring additional ablation therapy. Furthermore, any repositioning of the applicator during the ablation and the procedure for applicator removal (ie, use of tract ablation, fiber enclosure, or other closure devices) should be noted. Last, the frequency of use within a reported series of all ancillary procedures should be provided to establish the procedural complexity that is required to achieve a specific outcome. This will also formally differentiate more complex procedures (requiring more time, equipment, resources, and ultimately, reimbursement) from simpler procedures requiring less time, associated equipment costs, and risk.

Other Study Population Data to Be Reported

The study population should be rigorously described, including inclusion/exclusion criteria, tumor type and size, or other patient selection criteria. The degree of proof of disease required for entry into the study (ie, biopsy, imaging, or serologic criteria) should be clearly specified. Pretreatment evaluation also needs to be reported. In addition to an appropriate focus on anatomy (ie, the organ, tumor size, location, and number), the pretreatment evaluation should also include tumor stage (ie, spread elsewhere), patient comorbidities, age, gender, and overall clinical debility as outcomes such as mortality will depend on these factors. Obviously, a debilitated, cachectic patient with widespread metastases will have a worse outcome following liver ablation than an otherwise well patient.

Studies have also suggested the potential complementary effects of chemotherapy and radiation therapy on ablation efficacy. Hence, the administration of either of these therapies to patients enrolled in clinical trials of ablation should be specified. This should be further classified as having received the conventional oncologic therapies previously, around the time of ablation (within 1 month), or during the follow-up period. The specific therapy protocol, duration of therapy, and time interval in relation to ablation therapy should also be provided.

Accurate and Complete Delineation of Ablation Procedures

Substantial confusion and difficulty in comparing results has arisen regarding the success and complication rates due to the fact that patients may have had one or more tumors treated over multiple procedure sessions. Ideally, all four parameters (number of patients, tumors, treatment sessions, and ablations) should be reported whenever possible. Additionally, results are often reported for heterogeneous populations of patients for which varied rationales for the procedure (ie, cure vs palliation) or outcomes (ie, hepatic metastases vs hepatocellular carcinoma) have been reported. Stratification of patients into appropriate categories is therefore advised to avoid confusion and best facilitate extraction of clinically meaningful conclusions.

Minimizing Technical Jargon

Although substantial technical jargon and marketing terminology appear within our literature, these should not be used. For example, colloquial phrasing such as "lesioning" and "burning" are to be avoided when describing the application of thermal energy. The term "roll off" that describes the impedance control algorithm of a particular manufacturer's RF device should not be used.

Comparison with Other Treatments

Given that many reports of image-guided therapy, particularly with newer technologies, are relatively small case series, a major benefit of uniform reporting standards is the ability to perform meta-analyses of outcomes to compare therapies. Clinical research studies should be reported in such a manner that the results can be directly compared with various cancer therapies including other forms of image-guided ablation, surgery, radiation, and chemotherapy. The gold/reference standard in oncology is survival, disease-free survival, and quality of life stratified by disease stage and patient functional status. While studies addressing these outcomes after ablation are becoming increasingly available, nevertheless, there continue to be limited data addressing these issues for many diseases treated with image-guided ablation (94). Thus, we wish to stress the need for studies on an organ-by-organ and disease-by-disease basis. Randomized, controlled and blinded studies are considered the gold standard for pivotal studies and should be performed when possible (95). By the same token, we acknowledge both the very real obstacles to performing such studies (including patient recruitment, long periods of data collection, expense, multicenter organization, etc), as well as the benefit of reporting less robust forms of data including retrospective studies, case series, and case reports (96). Finally, in our current worldwide financial climate, we strongly encourage and advocate for the performance of both cost-effectiveness analysis and comparative effectiveness studies, recognizing that these are essential to optimally positioning tumor ablation in comparison with other available treatments (97,98).

Statistical Evaluation

Regardless of the study type, rigorous statistical evaluation appropriate for the data collected should be presented. The primary and secondary study end points should be clearly stated. Bearing in mind that the data from individual studies may need to be treated differently, in general survival outcomes should be reported using life-table (Kaplan-Meier) analysis. Patients should be randomized, if possible, and results reported based on intention to treat, treated as randomized, as treated per protocol (ie, excluding protocol violations). Outcomes may further need to be stratified according to multiple factors (tumor type, grade and stage, functional status, comorbidities, etc) Appropriate methodology for assessment of quality of life should be likewise selected (99).

More Relevant Studies

Since the original document, many additional relevant studies have been published. Appendix E1 (online) includes more relevant studies that could not be included because of article length limitations.

Conclusions

The original intent of this standardization of terminology was to provide an appropriate vehicle for reporting the various aspects of image-guided ablation therapy. Our intent continues to be to provide such a framework in order to facilitate the clearest communication between investigators, and the greatest flexibility in comparison among the many newer, exciting, and emerging technologies. Clearly, 10 years later, this is an ongoing process that will require that we adapt to our greater understanding of improving existing technologies and emerging novel treatments. As the original version of this document has been successful in providing a framework for the evaluation of ablation therapies worldwide, we encourage all of our colleagues to adopt the terminology and reporting strategies outlined in this updated proposal to facilitate worldwide communication of scientific advances.

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