UCSF UC San Francisco Previously Published Works

Title

Imaging of Anal Squamous Cell Carcinoma: Survey Results and Expert Opinion from the Rectal and Anal Cancer Disease-Focused Panel of the Society of Abdominal Radiology.

Permalink

https://escholarship.org/uc/item/3s4371j5

Journal Abdominal Radiology, 48(9)

Authors

Golia Pernicka, Jennifer Rauch, Gaiane Gangai, Natalie <u>et al.</u>

Publication Date

2023-09-01

DOI

10.1007/s00261-023-03863-8

Peer reviewed



HHS Public Access

Abdom Radiol (NY). Author manuscript; available in PMC 2024 March 12.

Published in final edited form as:

Author manuscript

Abdom Radiol (NY). 2023 September ; 48(9): 3022–3032. doi:10.1007/s00261-023-03863-8.

Imaging of Anal Squamous Cell Carcinoma: Survey Results and Expert Opinion from the Rectal and Anal Cancer Disease-Focused Panel of the Society of the Abdominal Radiology

Jennifer S. Golia Pernicka, MD¹, Gaiane M. Rauch, MD PhD², Natalie Gangai, MS¹, David D.B. Bates, MD¹, Randy Ernst, MD², Thomas A. Hope, MD³, Natally Horvat, MD PhD¹, Shannon P. Sheedy, MD⁴, Marc J. Gollub, MD¹

¹Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY, 10065, United States

²Department of Radiology, University of Texas MD Anderson Cancer Center, Houston, TX, United States

³Departments of Radiology and Biomedical Imaging and Pharmaceutical Chemistry, University of California San Francisco, San Francisco, CA, United States

⁴Department of Radiology, Mayo Clinic, Rochester, MN, United States

Abstract

The role and method of image-based staging of anal cancer has evolved with the rapid development of newer imaging modalities and the need to address the rising incidence of this rare cancer. In 2014, the European Society of Medical Oncology mandated pelvic magnetic resonance imaging (MRI) for anal cancer and subsequently other societies such as the National Comprehensive Cancer Network followed suit with similar recommendations. Nevertheless, great variability exists from center to center and even within individual centers. Notably, this is in stark contrast to the imaging of the anatomically nearby rectal cancer. As participating team members for this malignancy, we embarked on a comprehensive literature review of anal cancer imaging to understand the relative merits of these new technologies which developed after computed tomography (CT), e.g., MRI and positron emission tomography / computed tomography (PET/CT). The results of this literature review helped to inform our next stage: questionnaire development regarding the imaging of anal cancer. Next, we distributed the questionnaire to members of the Society of Abdominal Radiology (SAR) Rectal and Anal Disease-Focused Panel (DFP), a group of abdominal radiologists with special interest, experience, and expertise in rectal and anal cancer, to provide expert radiologist opinion on the appropriate anal cancer imaging strategy. In our expert opinion survey, experts advocated the use of MRI in general (65% overall and 91-100% for primary staging clinical scenarios) and acknowledged the superiority of PET/CT for nodal assessment (52-56% agreement for using PET/CT in primary staging clinical scenarios compared to 30% for using MRI). We therefore support the use of MRI and PET and

Corresponding Author: Jennifer S. Golia Pernicka, MD, 530 E 74th St, Room 07118, New York, NY 10021, (646) 608 1817, goliapej@mskcc.org.

Competing Interests: DDBB is a consultant for the Boston Imaging Core Lab. The remaining authors have no conflicts of interest to declare.

suggest further exploration of PET/MRI as an optimal combined evaluation. Our questionnaire responses emphasized the heterogeneity in imaging practice as performed at numerous academic cancer centers across the United States and underscore the need for further reconciliation and establishment of best imaging practice guidelines for optimized patient care in anal cancer.

Keywords

anal squamous cell carcinoma; anal cancer; magnetic resonance imaging; positron emission tomography / computed tomography; computed tomography; expert opinion

Introduction

Squamous cell carcinoma of the anus, also known as anal cancer, is a rare tumor representing 0.3% of new cancer cases worldwide, [1, 2], and has undergone a disturbing increase in incidence rate of about 2% per year over the past decade [2]. Important diagnostic and treatment-related differences exist between anal and rectal cancer despite their anatomic proximity. Rectal cancer requires magnetic resonance imaging (MRI) for staging and surgical planning. In contrast, anal cancer evolved from being treated primarily with surgery like rectal cancer into a predominantly non-surgical disease. This remarkable medical advance grew out of the landmark Nigro study in 1974 which achieved pathologic complete response rates of 75%–90% for anal cancer when treated with combined chemotherapy and radiation therapy followed by surgery [3].

Standard imaging for anal cancer staging initially consisted of endoanal ultrasound [4, 5] and computed tomography (CT), but In 2014, the European Society of Medical Oncology (ESMO) guidelines proposed pelvic MRI as **mandatory**, citing a need for the superior soft-tissue resolution provided by MRI [6]. Subsequently, many other societies followed suit in **recommending** pelvic MRI for anal cancer staging, including the Association of Coloproctology of Great Britain and Ireland, the American Society of Colorectal Surgeons in 2018, and the National Comprehensive Cancer Network (NCCN) in 2022 [7–11].

Although advances in imaging technology represent one of the most impactful medical discoveries in the past century and are credited with positively altering the management of patients, they may also increase cost and the risk of false positives which results in their decreased specificity and lower positive predictive value [12]. To wit, a recent anal cancer systematic review explored anecdotal observations by seasoned clinicians of increases in nodal stage and revealed [12] a documented nodal stage migration in anal cancer Surveillance, Epidemiology, and End Results (SEER) data over several decades. The authors reported that while there was a 7% increase in lymph node positivity every ten years over the last three decades, there was no concomitant change in survival. Indeed, groups of patients both with positive and negative lymph nodes showed an improved five-year survival rate. The authors therefore posited that advanced imaging may be one factor for staging misclassification and subsequent reduced prognostic discrimination. Admittedly, this hypothesis is hard to prove in this primarily non-surgical disease since pathologic proof of lymph node positivity is rarely available. However, new awareness of this stage-migration phenomenon (termed "Will Rogers Phenomenon") [12] prompted our group of

interested oncologic imagers, to explore the relative merits of MRI and positron emission tomography/computed tomography (PET/CT), especially as applied to nodal evaluation. We hypothesized that; perhaps a patient could be staged with only one of these modalities in the majority of cases. Moreover, unlike for rectal cancer, the available guidelines for anal cancer imaging are variable and often contradictory to one another, with some mandating pelvic MRI and others accepting CT or PET/CT as alternatives.

Thus, the goal of this literature review-based, questionnaire-informed expert opinion was to survey North American specialty academic radiologists with expertise in anal cancer imaging from recognized centers of medical excellence to propose the most appropriate anal cancer imaging strategy and bring the most relevant issues to the forefront as a first step for further discussion and collaborative investigation, particularly among treating oncologists.

Methods

Overview

To derive a baseline consensus expert opinion, the process we undertook was as follows:

Step 1 Literature search—A literature search was performed by a medical librarian at Memorial Sloan Kettering Cancer Center under the direction of the lead (MJG) and co-lead (JSGP) of the committee for literature review (details below). The medical librarian searched the PubMed database for relevant studies in the literature using structured methodology previously established by the MSK Evidenced-based Cancer Imaging Program whose role is to develop and implement standards for the use of advanced imaging. An elaborate list of Medical Subject Headings (MeSH) terms related to anal cancer imaging was used for the search, resulting in a total of 715 papers. See Online Resource 1 for the Evidentiary Review and list of MeSH terms.

Step 2 Literature review committee—The committee for literature review comprised members of the anal cancer sub-committee of the Society of Abdominal Radiology (SAR) Rectal and Anal Cancer Disease-Focused Panel who expressed interest in this project (MJG, JSGP, GMR, DDBB, RE, SPS, NH).

Step 3 Literature review screening form—An online screening form was developed for the purpose of the literature review and was agreed upon by the committee. See Online Resource 2 for the online screening form.

Step 4 Summarize literature review—The total number of final papers were divided evenly among members to read and summarize, the summary of which was filled out on the screening form.

Step 5 Online questionnaire—The committee for literature review developed an online questionnaire in the web-based Research Electronic Data Capture (REDCap) application (Vanderbilt University, TN). The starting point was a questionnaire template borrowed with permission and modified from the European Society of Gastrointestinal and

Abdominal Radiology (ESGAR) Rectal Cancer Guidelines [13] questionnaire available to one of the authors (MJG), a former member of that expert panel.

Step 6 Determine the expertise needed among the panel of questionnaire responders—An email invitation was sent to all 42 members of the SAR Rectal and Anal

Cancer Disease-Focused Panel on July 2, 2021, to assess expertise. The questions assessing expertise pertained to the volume of anal cancer cases read weekly, regular involvement in Colorectal Multidisciplinary Team meetings, service on various committees at the hospital/community/city/state/national/international level, and the number of published peer-reviewed articles on imaging and anal cancer.

Step 7 Online questionnaire distribution—The questionnaire was emailed to these 22 members on November 9, 2021. In addition to these 22 members who were all radiologists, the questionnaire was also emailed to five nuclear medicine physicians from members' collaborating institutions.

Step 8 Analyze the questionnaire results—Frequencies were used to assess categorical variables. Means and standard deviations were calculated to assess continuous variables. All analyses were conducted in SPSS version 26 (IBM, Armonk, NY).

RESULTS

1. Literature Search

Among 715 papers, the lead and co-lead of the committee for literature review subsequently deemed 154 papers to be relevant to imaging and anal cancer. See Online Resource 3 for the list of 154 papers.

2. Literature Review Committee

The authors (MJG, JSGP, GMR, DDBB, RE, SPS, NH) formed this committee.

3. Screening Form Development for Literature Review

The selected 154 papers were divided among the members of the committee who read and provided a synopsis of each article assigned to them using this screening form.

4. Literature Review by Committee

Of the 154 papers divided among the members of the committee for literature review, 45 were deemed not relevant to anal cancer imaging. Thus, the final database from which we drew conclusions for our baseline expert opinion included 109 papers from 1990 to 2020, which consisted of 47 retrospective studies, 21 prospective studies including 5 prospective trials (mean number of patients = 41; range, 11–115 patients), 25 review papers, 10 guideline papers, 3 meta-analyses, and 3 expert reviews. See Figure 1 for the flow of inclusion of papers. Of the 109 final papers, eight papers were determined to be of the highest quality for evidence regarding the use of imaging in anal cancer based on the committee members' general knowledge of levels of evidence strata. These eight papers were subsequently formally graded by the medical librarian using the Oxford Centre for

Highlights from this literature review are presented below:

1. Level 1 evidence:

level-4 papers, and one level-5 paper.

- A meta-analysis [15] showed that PET/CT is highly specific for the detection of locoregional nodal involvement (patient-level pooled specificity = 90%; 95% CI: 86%–93%), with some loss of specificity in the inguinal nodes. However, the sensitivity of PET/CT was low, which could be due to the peri-rectal nodes being over-shadowed by intense FDG uptake of the primary mass (patient-level pooled sensitivity = 56%; 95% CI: 45%–67%). As such, the authors suggested the need for MRI to detect small nodes missed by PET/CT.
- **2.** Level 4/5 evidence:
 - According to one meta-analysis, PET/CT scanning may detect distant metastases not noted on CT or MRI in approximately 2%–5% cases. In addition, PET/CT upstaged 5%–38% of patients and downstaged 8%–27% of patients compared to conventional imaging, leading to changes in management in 13%–60% of patients [16].
 - In the clinical practice guidelines jointly authored by ESMO, the European Society of Surgical Oncology (ESSO), and the European Society of Radiotherapy and Oncology (ESTRO), the authors note that for T-categorization, CT has poor soft-tissue contrast and is inadequate. On the other hand, pelvic MRI provides better soft tissue contrast resolution of the anal canal and has been incorporated since 2010 [6].
 - Nodal assessment is limited with MRI; it is improved with PET/CT (sensitivity of 93% and specificity of 76% vs. MRI 89% and 62%) [17–23].
 - PET/CT is also useful for the assessment of metabolic tumor activity, allowing for prognostication and the delineation of radiation target volumes [24, 25].
 - Post-treatment imaging is not standardized, and clinical complete response remains determined by traditional clinical assessment [26]. However, for incomplete responders, MRI of the pelvis for surgical planning and PET/CT to exclude distant metastases are recommended.

In summary, the literature review revealed that diagnostic imaging for anal cancer strongly favors PET/CT for nodal staging; however, clear evidence to support MRI for either staging of the primary tumor or lymph nodes is lacking, despite the leanings of multiple society recommendations. The difference seen between the literature and clinical practice regarding the imaging of anal cancer set the stage for the development of an online

questionnaire distributed among our expert radiology colleagues in an attempt to reconcile this discrepancy.

5. Questionnaire Development

See Online Resource 4 for the questionnaire.

6. Determination of Expertise and Panel Selection, and Online Distribution of Questionnaire

A total of 22/42 (52.4%) members responded yes to the questionnaire, with specific details of expertise in Table 1.

7. Distribute Questionnaire:

Of the 27 experts who were emailed the questionnaire, 23 filled out the online questionnaire. See Table 1 for the characteristics of respondents and see Figure 2 for a map of their respective geographic locations across the United States.

8. Analysis of Questionnaire Results:

Imaging Modalities for Locoregional Staging of Anal Cancer—The respondents ranked MRI as their first-choice modality for T categorization, both for primary (baseline) staging including overall locoregional nodal staging, estimation of size, and evaluation of palpably large T3 and T4 tumors (91%–100% agreement), and for follow-up assessment including restaging, final response assessment after 6–12 months, and evaluation of suspected recurrence (52%–60% agreement). While high levels of agreement were not reached for N categorization, PET/CT was the majority first-choice modality for baseline N categorization in both the HIV– and HIV+ populations (52%–56% agreement) as well as in the follow-up post-CRT setting (69% agreement). Detailed results of the questionnaire pertaining to the choice of imaging modalities for locoregional staging of anal cancer is given in Table 2.

MRI Acquisition, Interpretation, and Reporting—Regarding MRI acquisition, there was a high level of agreement on 1.5 T as the required field strength (100% agreement) and the use of an external surface coil (95% agreement). Of the various MRI sequences to be performed, the majority rated that obtaining multiplanar 2D T2-weighted (T2W) sequences and diffusion-weighted imaging (DWI) sequences would be very helpful or extremely helpful (T2W: 86–90% agreement; DWI: 95% agreement). When asked about the optimal slice thickness on T2W, all agreed on a slice thickness of 4 mm (100% agreement) although there was also a high level of agreement on a slice thickness of 3 mm (91% agreement).

Regarding the criteria for MRI interpretation, there was a high level of agreement for using lymph node morphology including border characteristics, signal heterogeneity, and shape to determine nodal involvement (95%-100% agreement). Responders also agreed on a size threshold > 10 mm for the external iliac nodes (78% agreement) and a size threshold > 10 mm for the inguinal nodes (83% agreement) to determine nodal involvement. On the

Regarding MRI reporting, the respondents agreed that mandatory elements to include on both baseline and restaging radiology reports are tumor length (100% agreement), T category (100% agreement for baseline and 57% agreement for restaging), any organ invasion (86%–95% agreement), presence of a fistula (86%–95% agreement), and N category (100% agreement for baseline and 71% for restaging). The presence of residual tumor and fibrosis was a recommended element on restaging radiology reports (95%–100% agreement).

Full results pertaining to MRI technique, imaging interpretation criteria, and reporting are highlighted in Table 3.

Discussion

We crafted and administered an online questionnaire surveying the opinion of radiologists specialized in abdominal/gastrointestinal imaging and of nuclear medicine physicians, to establish expert opinion regarding the optimal imaging of anal cancer. MRI was the preferred modality overall for the evaluation of the primary tumor and locoregional N categorization at all timepoints including: baseline, immediate restaging post CRT, response assessment 6–12 months post CRT, and at times of suspected recurrence. On the other hand, PET/CT was favored specifically for N categorization in the baseline setting in both the HIV– and HIV+ populations, as well as in the post-CRT setting. Our online questionnaire also revealed consensus with regards to MRI acquisition, interpretation criteria, and reporting in the imaging of anal cancer, which we propose for widespread adoption to promote standardization, similar to what has been done for rectal cancer through various society guidelines and white paper publications [13, 27].

MRI might have evolved to be the preferred choice for the imaging of anal cancer among radiologists by virtue of increasing availability and superior soft tissue resolution of the primary tumor. Momentum was probably gained after the United Kingdom made pelvic MRI mandatory for rectal cancer evaluation (and is universally covered by the National Health Service) as promulgated by ESMO in 2010. The ESMO guidelines were ostensibly based on three retrospective descriptive series totaling 77 patients [28–30] and possibly informal extrapolation from the beneficial contributions of pelvic MRI being experienced in rectal cancer. A review comparing the discrepancies between NCCN and ESMO guidelines states that while the recommendations for the *treatment* of anal cancer in both guidelines stem from high-level evidence, the recommendations for staging and surveillance are "based on little to no evidence" [31].

While many societies mandate pelvic MRI as the first choice for the imaging of anal cancer (with the joint ESMO–ESTRO guidelines [6] as a notable example), other societies worldwide have not followed suit, perhaps due to local practice patterns but also due to the lack of robust scientific evidence for the use of MRI over CT or PET/CT. For example, NCCN guidelines suggest a workup including "pelvic CT or MRI" [11]. While

studies have shown that MRI is useful for the evaluation of the primary tumor and of the locoregional nodes [29], assessment of response [32], and prediction of recurrence and outcomes following CRT [33], as well as that DWI is useful as a prognostic biomarker [34], there is a lack of studies directly comparing the imaging modalities.

The only study involving a direct comparison of imaging modalities for the imaging of anal cancer was a retrospective study involving 54 patients who underwent both PET/CT and MRI [24]. This study revealed that additional data from PET/CT led to changes in management in 13/54 (24%) patients. Of the 13 patients who had a change in management, in 10 patients, 15 additional suspicious inguinal and external iliac nodes were detected, increasing N categorization; in 2 patients, three inguinal nodes had no tracer uptake but were felt to be suspicious at MRI, decreasing the N category; and in 1 patient, liver metastasis detection (due to full body imaging compared with MRI presumably), increasing the M category. When the authors evaluated discordant PET/CT and MRI findings, they found that 13/54 (24%) patients had "missing or discrepant" data on PET/CT compared with MRI. Of these 13 patients, in 7 patients, perirectal nodes were missed due to small size (less than 6 mm) but were adjacent to the primary tumor (an area already encompassed in the radiation field), decreasing the N category; in 6 patients, the T category changed due to different size estimations (2 larger and 2 smaller at PET); and in 2 patients, PET was unable to detect organ invasion (T4), albeit this did not change radiation dose. Ultimately, based on histopathology and clinical follow up, it was determined that in 7/54 patients (13%), these discrepancies favored PET as more accurate, and in 6/54 (11.2%) patients, MRI was favored to be more accurate. The numbers were too small to make any conclusions on changes in treatment. Another study compared the impact of different MRI sequences (i.e., T2W vs. DWI) on T categorization [35] but did not compare different modalities.

Since there is a dearth of studies directly comparing imaging modalities—due to the lack of a pathologic reference standard in anal cancer; a disease primarily treated with definitive chemoradiation—our efforts aimed at establishing expert opinion drawing consensus from imaging experts across the United States based on their subspecialty experience. Expert opinion in no way can replace the rigor of scientific study and we recognize the strong need for studies directly comparing the relative efficacy of MRI and PET/CT as well as their cost-effectiveness. While expert opinion and consensus papers have been published in rectal cancer and other tumors [13, 27], we believe ours is the first of its kind in anal cancer.

Pending high level evidence, what might the next steps be in sorting out these issues pertaining to the imaging of anal cancer? Why not perform PET/CT and MRI in all? While many tumors require multimodality imaging, we believe that an attempt at refinement is warranted to avoid over-imaging, avoid misclassification of lymph nodes, promote a standardized diagnostic approach, and to take into consideration unnecessary costs of advanced imaging if it is indeed superfluous. This survey and expert opinion represent a first step and indicate that more work needs to be done and that the optimal imaging protocol for anal cancer is yet to be determined. As an example, one could contemplate that a routine CT scan showing suspicious pelvic lymph nodes might triage a patient towards PET/CT in lieu of MRI, whereas one showing a bulky primary tumor invading the vagina might triage a

patient towards MRI in lieu of PET/CT, rather than reflexively obtaining all imaging in both cases.

In our expert opinion survey, experts advocated the use of MRI in general but acknowledged the superiority of PET/CT for nodal assessment, falling in line with the literature indicating that PET/CT is superior for nodal status. We hope that this exploration as well as further research by other groups will spur more interest and greater discussion in the medical community as to the optimal imaging strategy for anal cancer. Furthermore, concerning the topic of imaging modalities for treatment planning, which was not formally surveyed here, more data are needed to determine which simulation (treatment planning) modality will prove most efficacious and result in the least collateral organ damage, highest overall survival, and lowest long-term morbidity. Lastly, with the increased availability of PET/MRI in the future, it may prove to be the ideal modality for staging, restaging, and radiation planning of anal cancer across a majority of clinical scenarios; however, more studies are needed to assess the added value of PET/MRI over PET/CT, including those that would investigate their cost-effectiveness.

The limitations of our questionnaire largely stem from bias, similar to other questionnairetype research. Sampling bias may have occurred in that we did not reach as many nuclear medicine physicians who are experts in reading PET/CT as we did diagnostic radiologists. Thus, we may have had under-represented expertise in PET/CT. Nevertheless, most of the diagnostic radiologists who responded to the questionnaire also have had some training in PET and actively present and discuss all imaging modalities including PET at dedicated multidisciplinary meetings. Additional bias may exist in the form of questionnaire bias, namely question design, questionnaire design (i.e., too lengthy), and the method of administration (i.e., online via REDcap).

Conclusion

While our investigation shows some consensus on several aspects of the imaging of anal cancer among imaging experts, there was also a lack of substantial agreement across multiple other aspects, speaking to the dearth of information available for us to make informed decisions and recommendations regarding the best and/or most accurate imaging strategy. We hope this expert opinion may serve to inform imaging recommendations amongst caretakers involved in anal cancer treatment. Future studies must be performed to support these initial recommendations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

The authors would like to thank Kendra Godwin and Andrew Chua for their help in the literature review process; Doenja Lembregts MD, PhD, for her help in organizing and displaying the data results, and Joanne Chin for her help in preparation of the manuscript.

Funding:

References

- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209–49. doi: 10.3322/caac.21660. [PubMed: 33538338]
- 2. National Cancer Institute Surveillance E, and End Results Program (SEER): Cancer Stat Facts: Anal Cancer. https://seer.cancer.gov/statfacts/html/anus.html (2022). Accessed April 12, 2022.
- Nigro ND, Vaitkevicius VK, Considine B, Jr. Combined therapy for cancer of the anal canal: a preliminary report. Dis Colon Rectum. 1974;17(3):354–6. doi: 10.1007/BF02586980. [PubMed: 4830803]
- Tarantino D, Bernstein MA. Endoanal ultrasound in the staging and management of squamous-cell carcinoma of the anal canal: potential implications of a new ultrasound staging system. Dis Colon Rectum. 2002;45(1):16–22. doi: 10.1007/s10350-004-6108-1. [PubMed: 11786758]
- 5. Herzog U, Boss M, Spichtin HP. Endoanal ultrasonography in the follow-up of anal carcinoma. Surg Endosc. 1994;8(10):1186–9. doi: 10.1007/bf00591047. [PubMed: 7809802]
- Glynne-Jones R, Nilsson PJ, Aschele C, Goh V, Peiffert D, Cervantes A, et al. Anal cancer: ESMO-ESSO-ESTRO clinical practice guidelines for diagnosis, treatment and follow-up. Eur J Surg Oncol. 2014;40(10):1165–76. doi: 10.1016/j.ejso.2014.07.030. [PubMed: 25239441]
- Geh I, Gollins S, Renehan A, Scholefield J, Goh V, Prezzi D, et al. Association of Coloproctology of Great Britain & Ireland (ACPGBI): Guidelines for the Management of Cancer of the Colon, Rectum and Anus (2017) - Anal Cancer. Colorectal Dis. 2017;19 Suppl 1:82–97. doi: 10.1111/codi.13709. [PubMed: 28632308]
- Moureau-Zabotto L, Vendrely V, Abramowitz L, Borg C, Francois E, Goere D, et al. Anal cancer: French Intergroup Clinical Practice Guidelines for diagnosis, treatment and follow-up (SNFGE, FFCD, GERCOR, UNICANCER, SFCD, SFED, SFRO, SNFCP). Dig Liver Dis. 2017;49(8):831– 40. doi: 10.1016/j.dld.2017.05.011. [PubMed: 28610905]
- Stewart DB, Gaertner WB, Glasgow SC, Herzig DO, Feingold D, Steele SR, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for Anal Squamous Cell Cancers (Revised 2018). Dis Colon Rectum. 2018;61(7):755–74. doi: 10.1097/DCR.000000000001114. [PubMed: 29878949]
- Rao S, Guren MG, Khan K, Brown G, Renehan AG, Steigen SE, et al. Anal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up(). Ann Oncol. 2021;32(9):1087–100. doi: 10.1016/j.annonc.2021.06.015. [PubMed: 34175386]
- NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]): Anal Carcinoma V.1.2022. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf (2022). Accessed April 12, 2022.
- Sekhar H, Zwahlen M, Trelle S, Malcomson L, Kochhar R, Saunders MP, et al. Nodal stage migration and prognosis in anal cancer: a systematic review, meta-regression, and simulation study. Lancet Oncol. 2017;18(10):1348–59. doi: 10.1016/S1470-2045(17)30456-4. [PubMed: 28802802]
- Beets-Tan RGH, Lambregts DMJ, Maas M, Bipat S, Barbaro B, Curvo-Semedo L, et al. Magnetic resonance imaging for clinical management of rectal cancer: Updated recommendations from the 2016 European Society of Gastrointestinal and Abdominal Radiology (ESGAR) consensus meeting. Eur Radiol. 2018;28(4):1465–75. doi: 10.1007/s00330-017-5026-2. [PubMed: 29043428]
- Oxford Centre for Evidence-Based Medicine: Oxford Centre for Evidence-Based Medicine: Levels
 of Evidence (March 2009). https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxfordcentre-for-evidence-based-medicine-levels-of-evidence-march-2009 (2009). Accessed April 12,
 2022.
- 15. Caldarella C, Annunziata S, Treglia G, Sadeghi R, Ayati N, Giovanella L. Diagnostic performance of positron emission tomography/computed tomography using fluorine-18 fluorodeoxyglucose in detecting locoregional nodal involvement in patients with anal canal cancer: a systematic

review and meta-analysis. ScientificWorldJournal. 2014;2014:196068. doi: 10.1155/2014/196068. [PubMed: 24672298]

- Mahmud A, Poon R, Jonker D. PET imaging in anal canal cancer: a systematic review and metaanalysis. Br J Radiol. 2017;90(1080):20170370. doi: 10.1259/bjr.20170370. [PubMed: 28972796]
- Winton E, Heriot AG, Ng M, Hicks RJ, Hogg A, Milner A, et al. The impact of 18fluorodeoxyglucose positron emission tomography on the staging, management and outcome of anal cancer. Br J Cancer. 2009;100(5):693–700. doi: 10.1038/sj.bjc.6604897. [PubMed: 19259091]
- Duimering A, Riauka T, Nijjar Y, Ghosh S, MacEwan R, Warkentin H, et al. Prognostic utility of pre- and post-treatment FDG-PET parameters in anal squamous cell carcinoma. Radiother Oncol. 2019;136:21–8. doi: 10.1016/j.radonc.2019.03.014. [PubMed: 31015125]
- Leccisotti L, Manfrida S, Barone R, Ripani D, Tagliaferri L, Masiello V, et al. The prognostic role of FDG PET/CT before combined radio-chemotherapy in anal cancer patients. Ann Nucl Med. 2020;34(1):65–73. doi: 10.1007/s12149-019-01416-y. [PubMed: 31728763]
- Rusten E, Rekstad BL, Undseth C, Klotz D, Hernes E, Guren MG, et al. Anal cancer chemoradiotherapy outcome prediction using (18)F-fluorodeoxyglucose positron emission tomography and clinicopathological factors. Br J Radiol. 2019;92(1097):20181006. doi: 10.1259/ bjr.20181006. [PubMed: 30810343]
- Kidd EA, Dehdashti F, Siegel BA, Grigsby PW. Anal cancer maximum F-18 fluorodeoxyglucose uptake on positron emission tomography is correlated with prognosis. Radiother Oncol. 2010;95(3):288–91. doi: 10.1016/j.radonc.2010.02.019. [PubMed: 20231040]
- 22. Deantonio L, Milia ME, Cena T, Sacchetti G, Perotti C, Brambilla M, et al. Anal cancer FDG-PET standard uptake value: correlation with tumor characteristics, treatment response and survival. Radiol Med. 2016;121(1):54–9. doi: 10.1007/s11547-015-0562-9. [PubMed: 26126968]
- Sadeghi R, Harsini S, Qodsi Rad MA, Dabbagh VR, Treglia G. Prognostic Significance of Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography in Anal Squamous Cell Carcinoma: A Systematic Review and a Meta-Analysis. Contrast Media Mol Imaging. 2018;2018:9760492. doi: 10.1155/2018/9760492. [PubMed: 30627062]
- Manafi-Farid R, Kupferthaler A, Wundsam H, Gruber G, Vali R, Venhoda C, et al. Additional Value of 2-[(18)F]FDG PET/CT Comparing to MRI in Treatment Approach of Anal Cancer Patients. J Clin Med. 2020;9(9). doi: 10.3390/jcm9092715.
- Rusten E, Rekstad BL, Undseth C, Al-Haidari G, Hanekamp B, Hernes E, et al. Target volume delineation of anal cancer based on magnetic resonance imaging or positron emission tomography. Radiat Oncol. 2017;12(1):147. doi: 10.1186/s13014-017-0883-z. [PubMed: 28874205]
- 26. James RD, Glynne-Jones R, Meadows HM, Cunningham D, Myint AS, Saunders MP, et al. Mitomycin or cisplatin chemoradiation with or without maintenance chemotherapy for treatment of squamous-cell carcinoma of the anus (ACT II): a randomised, phase 3, open-label, 2 × 2 factorial trial. Lancet Oncol. 2013;14(6):516–24. doi: 10.1016/S1470-2045(13)70086-X. [PubMed: 23578724]
- Gollub MJ, Arya S, Beets-Tan RG, dePrisco G, Gonen M, Jhaveri K, et al. Use of magnetic resonance imaging in rectal cancer patients: Society of Abdominal Radiology (SAR) rectal cancer disease-focused panel (DFP) recommendations 2017. Abdom Radiol (NY). 2018;43(11):2893– 902. doi: 10.1007/s00261-018-1642-9. [PubMed: 29785540]
- Goh V, Gollub FK, Liaw J, Wellsted D, Przybytniak I, Padhani AR, et al. Magnetic resonance imaging assessment of squamous cell carcinoma of the anal canal before and after chemoradiation: can MRI predict for eventual clinical outcome? Int J Radiat Oncol Biol Phys. 2010;78(3):715–21. doi: 10.1016/j.ijrobp.2009.08.055. [PubMed: 20171812]
- Koh DM, Dzik-Jurasz A, O'Neill B, Tait D, Husband JE, Brown G. Pelvic phased-array MR imaging of anal carcinoma before and after chemoradiation. Br J Radiol. 2008;81(962):91–8. doi: 10.1259/bjr/96187638. [PubMed: 18238920]
- Roach SC, Hulse PA, Moulding FJ, Wilson R, Carrington BM. Magnetic resonance imaging of anal cancer. Clin Radiol. 2005;60(10):1111–9. doi: 10.1016/j.crad.2005.05.008. [PubMed: 16179172]

- Johnson N, Pellino G, Simillis C, Qiu S, Nikolaou S, Baird DL, et al. Discrepancies between NCCN and ESMO guidelines in the management of anal cancer: a qualitative review. Updates Surg. 2017;69(3):345–9. doi: 10.1007/s13304-017-0470-8. [PubMed: 28597183]
- Gourtsoyianni S, Goh V. MRI of anal cancer: assessing response to definitive chemoradiotherapy. Abdom Imaging. 2014;39(1):2–17. doi: 10.1007/s00261-013-0032-6. [PubMed: 24072381]
- Owczarczyk K, Prezzi D, Cascino M, Kozarski R, Gaya A, Siddique M, et al. MRI heterogeneity analysis for prediction of recurrence and disease free survival in anal cancer. Radiother Oncol. 2019;134:119–26. doi: 10.1016/j.radonc.2019.01.022. [PubMed: 31005205]
- 34. Muirhead R, Bulte D, Cooke R, Chu KY, Durrant L, Goh V, et al. A Prospective Study of Diffusion-weighted Magnetic Resonance Imaging as an Early Prognostic Biomarker in Chemoradiotherapy in Squamous Cell Carcinomas of the Anus. Clin Oncol (R Coll Radiol). 2020;32(12):874–83. doi: 10.1016/j.clon.2020.09.003. [PubMed: 33023818]
- 35. Prezzi D, Mandegaran R, Gourtsoyianni S, Owczarczyk K, Gaya A, Glynne-Jones R, et al. The impact of MRI sequence on tumour staging and gross tumour volume delineation in squamous cell carcinoma of the anal canal. Eur Radiol. 2018;28(4):1512–9. doi: 10.1007/s00330-017-5133-0. [PubMed: 29134349]



Fig. 1.

Inclusion of Papers for the Literature Review Concerning Imaging Modalities in Anal Cancer.





Table 1.

Characteristics of Questionnaire Respondents (n = 23)

Characteristic	Number	
Type or radiologist		
Diagnostic radiologist (MRI, CT)	20 (87%)	
Nuclear medicine radiologist (PET/CT)	2 (9%)	
Both (MRI, CT, PET/CT)	1 (4%)	
Dedicated abdominal radiologist		
Yes	22 (96%)	
No	1 (4%)	
Participate in colorectal multidisciplinary team meetings		
Yes	23 (100%)	
No	0 (0%)	
Participate on a committee (hospital, community, city/state, national, international) related to anal cancer ^a		
Yes	15 (65%)	
No	8 (35%)	
Mean (standard deviation) number of anal cancer cases read per year on imaging		
MRI	62 (48)	
СТ	32 (24)	
PET/CT	34 (20)	
Mean number of papers ever published on anal cancer	1 (1)	

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography

^aFor example: American Joint Committee on Cancer (AJCC), Society of Abdominal Radiology, International Rare Cancers Initiative (IRCI), Groupe de REcherche en Radiologie sur le CAncer du Rectum (GRERCAR)

Table 2.

Imaging Modalities for Locoregional Staging of Anal Cancer

Statement		Level of agreement	Remarks		
Primary staging (baseline staging including overall locoregional staging, estimation of size, and evaluation of palpably large T3 and T4 tumors):					
First Choice Modality					
Overall	MRI	65%			
T-staging	MRI	91–100%			
N-staging	PET/CT or MRI	52-56% (PET/CT) vs 30% (MRI)	Similar results for HIV+ and HIV- cases		
Second Choice Modality					
Overall	PET/CT or CT	43% (PET/CT) vs 35% (CT)			
T-staging	CT or PET/CT	52-61% (CT) vs 35-48% (PET/CT)	CT mainly preferred (61%) for T3-4 tumors		
N-staging	Undecided	44–52% MRI vs 26–30% CT vs 17–21% PET/CT	Similar results for HIV+ and HIV- cases		
Follow-up (restaging, final response assessment after 6–12 months ^a , suspected recurrence)					
First Choice Modality	MRI	52%-60%	Except for nodal restaging after CRT (69% PET/CT)		
Second Choice Modality	PET/CT	44%-48%	39%-48% indicated PET/CT as first choice		
Other modalities:					
- EAUS is not routinely used at the participants' institutions (4%-34% yes; 13%-39% no; 43%-69% do not know)					
- Lymphoscintigraphy is not routinely used for lymph node assessment at the participants' institutions (0%–13% yes; 30% no; 56%–69% do not know)					

Abbreviations: CT, computed tomography; EAUS, endoanal ultrasound; MRI, magnetic resonance imaging; PET, positron emission tomography

 $a^{69\%}$ of participants indicated that response assessment after 6–12 months is routinely performed at their institution (17% were unsure)

Table 3.

MRI Acquisition, Interpretation Criteria, and Reporting

Statement		Level of agreement	Remarks		
Hardware & patient preparation					
Required field strength:	1.5T	100%	No preference for 1.5T or 3.0T		
Recommended coil type:	External surface coil	95%			
Patient preparation:	•	:	•		
- Would include a spasmolytic agent		52% no			
- Would include a preparatory enema		67% no			
- Would recommend endorectal filling		95% no			
Imaging sequences					
Recommended:					
- Multiplanar 2D T2W sequences (sagittal, coronal, transverse)		86%–90% very helpful or extremely helpful			
Recommended slice thickness 4 mm		100%	91% recommend 3 mm		
Recommended sequence angulation (relative to tumor axis or anal canal)		57% yes			
- Diffusion-weighted sequence		95% very helpful or extremely helpful			
Optional (in order of importance):					
- Contrast-enhanced T1-weighted sequence		52% very helpful or extremely helpful; 38% moderately helpful; 10% slightly helpful			
- Dynamic contrast-enhanced sequence		29% very helpful or extremely helpful; 29% moderately helpful; 33% slightly helpful			
- Fat suppressed / STIR sequence		19% very helpful or extremely helpful; 24% moderately helpful; 33% slightly helpful			
- Unenhanced T1-weighted sequence		19% moderately helpful; 67% slightly helpful			
First-choice imaging sequence(s) for th	e assessment of:				
T-category (baseline)	2D T2W	86%–91%	No preference for sagittal, coronal, or transverse		
N-category (baseline)	Transverse 2D T2W	81%	14% DWI		
yT-category (restaging): yT0 vs yT+	Transverse 2D T2W or DWI	48% DWI; 43% T2W			
yN-category (restaging)	Transverse 2D T2W	71%	24% DWI		
Reporting checklist					
Mandatory to include in baseline and r	estaging report:				
Tumor length		100%			
T category		100%	Optional in restaging setting (57%)		
Organ invasion		86%-95%			
N category		100%	Optional in restaging setting (71%)		
Presence of lateral N+ nodes		90%-95%			

Statement	Level of agreement	Remarks		
Presence of inguinal N+ nodes	95%			
Presence of residual tumor and fibrosis (note: restaging report only)	95%-100%			
Presence of fistula	86%-90%			
Optional to include in baseline and restaging report:				
Circumferential location within bowel wall (lateral, anterior, posterior)	76%			
Circumferential growth (from to o'clock)	57%-62%			
Number of suspicious lymph nodes	48%-67%	Baseline 48%; restaging 67%		
Morphological pattern of tumor growth	43%-48%			
Criteria for image interpretation				
Primary N staging – recommended criteria for N+				
Size	86%			
Size threshold for mesorectal nodes	Undecided	44% > 5 mm; 39% > 7 mm; 17% > 10 mm		
Size threshold for internal iliac / obturator nodes	Undecided	17% > 5 mm; 56% > 7 mm; 27% > 10 mm		
Size threshold for external iliac nodes	> 10 mm (78%)			
Size threshold for inguinal nodes	> 10 mm (83%)			
Morphology (border characteristics, signal heterogeneity and shape)	95%-100%			
Presence of necrosis	95%			
(Optional: enhancement patterns)	52%			
Restaging local tumor stage after CRT				
Hypointense fibrotic residue (without iso-intense mass) is indicative of yT0	91%			
Criteria for restaging of yN-category / diagnosing yN0 after CRT				
Size / reduction in size	Undecided	19%–33% yes; 14%–24% no; 48%–53% do not know		
Normalization of morphology (sharp border, homogeneous signal, oval shape)	Undecided	14%–24% yes; 14%–24% no; 48%–57% do not know		

Abbreviations: CT, computed tomography; CRT, chemoradiation therapy; DWI, diffusion-weighted imaging; EAUS, endoanal ultrasound; MRI, magnetic resonance imaging; PET, positron emission tomography; T2W, T2-weighted imaging