PET/MR in Head and Neck Cancer - An Update

Huellner, Martin W

Abstract: In academic centers, PET/MR has taken the road to clinical nuclear medicine in the past 6 years since the last review on its applications in head and neck cancer patients in this journal. Meanwhile, older sequential PET + MR machines have largely vanished from clinical sites, being replaced by integrated simultaneous PET/MR scanners. Evidence from several studies suggests that PET/MR overall performs equally well as PET/CT in the staging and restaging of head and neck cancer and in radiation therapy planning. PET/MR appears to offer advantages in the characterization and prognostication of head and neck malignancies through multiparametric imaging, which demands an exact preparation and validation of imaging modalities, however. The majority of available clinical PET/MR studies today covers FDG imaging of squamous cell carcinoma arising from a broad spectrum of locations in the upper aerodigestive tract. In the future, specific PET/MR studies are desired that address specific histopathological tumor entities, nonepithelial malignancies, such as major salivary gland tumors, squamous cell carcinomas arising in specific locations, and malignancies imaged with non-FDG radiotracers. With the advent of digital PET/CT scanners, PET/MR is expected to partake in future technical developments, such as novel iterative reconstruction techniques and deviceless motion correction for respiration and gross movement in the head and neck region. Owing to the still comparably high costs of PET/MR scanners and facility requirements on the one hand, and the concentration of multidisciplinary head and neck cancer treatment mainly at academic centers on the other hand, a more widespread use of this imaging modality outside major hospitals is currently limited.

DOI: https://doi.org/10.1053/j.semnuclmed.2020.07.006

Posted at the Zurich Open Repository and Archive, University of Zurich
ZORA URL: https://doi.org/10.5167/uzh-196080
Journal Article
Published Version

The following work is licensed under a Creative Commons: Attribution 4.0 International (CC BY 4.0) License.

Originally published at:
Huellner, Martin W (2021). PET/MR in Head and Neck Cancer - An Update. Seminars in Nuclear Medicine, 51(1):26-38.
DOI: https://doi.org/10.1053/j.semnuclmed.2020.07.006
PET/MR in Head and Neck Cancer – An Update

Martin W. Huellner, MD

In academic centers, PET/MR has taken the road to clinical nuclear medicine in the past 6 years since the last review on its applications in head and neck cancer patients in this journal. Meanwhile, older sequential PET + MR machines have largely vanished from clinical sites, being replaced by integrated simultaneous PET/MR scanners. Evidence from several studies suggests that PET/MR overall performs equally well as PET/CT in the staging and restaging of head and neck cancer and in radiation therapy planning. PET/MR appears to offer advantages in the characterization and prognostication of head and neck malignancies through multiparametric imaging, which demands an exact preparation and validation of imaging modalities, however. The majority of available clinical PET/MR studies today covers FDG imaging of squamous cell carcinoma arising from a broad spectrum of locations in the upper aerodigestive tract. In the future, specific PET/MR studies are desired that address specific histopathological tumor entities, nonepithelial malignancies, such as major salivary gland tumors, squamous cell carcinomas arising in specific locations, and malignancies imaged with non-FDG radiotracers.

With the advent of digital PET/CT scanners, PET/MR is expected to partake in future technical developments, such as novel iterative reconstruction techniques and deviceless motion correction for respiration and gross movement in the head and neck region. Owing to the still comparably high costs of PET/MR scanners and facility requirements on the one hand, and the concentration of multidisciplinary head and neck cancer treatment mainly at academic centers on the other hand, a more widespread use of this imaging modality outside major hospitals is currently limited.

Semin Nucl Med 51:26-38 © 2020 The Author. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

PET/MR Protocols

In order to ensure acceptance of a positron emission tomography/magnetic resonance (PET/MR) examination both by patients and by referring physicians, its acquisition time should roughly not exceed the acquisition time of a full head and neck MR protocol. Such a fully diagnostic MR protocol is usually in the range of 30-40 minutes. Furthermore, the PET/MR acquisition time should fit within an examination slot allotted for positron emission tomography / computed tomography (PET/CT). A diagnostic PET/MR scan in head and neck cancer patients consists of a regionalized MR scan covering the head and neck, and a whole-body PET/MR scan covering the area from the vertex of the skull to the mid-thighs.

The head and neck MR scan should be acquired preferentially during the last minutes of the uptake phase in order to meet the patient’s in-house time with a PET/CT examination. Whenever possible, the regionalized MR scan should be gadolinium contrast-enhanced, with the ulterior motive of providing highest diagnostic accuracy and saving the patient an additional separate MR examination. Examination time may be saved instead by refraining from diffusion-weighted pulse sequences and perfusion-weighted pulse sequences, whose diagnostic yield and clinical impact appear to be limited in the presence of PET data, although controversy exists on this matter. Time may also be saved by limiting the usually fat-suppressed T2-weighted MR pulse sequences to only one single plane, typically axial, and the T1-weighted contrast-enhanced fat-suppressed MR

Address reprint requests to Martin W. Huellner, MD, Section Head PET/CT/MR Imaging, Department of Nuclear Medicine, University Hospital Zurich/University of Zurich, Rämistrasse 100, CH-8091, Zurich, Switzerland. E-mail: martin.huellner@usz.ch

https://doi.org/10.1053/j.semnuclmed.2020.07.006
0001-2998/© 2020 The Author. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
pulse sequences to the axial plane and another plane (coronal or sagittal, depending mainly on the location of the primary tumor). Hence, the minimum requirements consist of the following MR pulse sequences: T1-weighted non-enhanced (axial), T2-weighted fat-suppressed (axial), T1-weighted contrast-enhanced fat-suppressed (axial + coronal/sagittal). Specific protocols may vary depending on the exact clinical question, the location and extent of the primary tumor and regional metastases (eg, skull base tumors, sinonasal tumors, possible vessel infiltration).

The whole-body PET/MR scan usually consists of several bins or body sections of a Dixon-type T1-weighted MR pulse sequence, such as Liver Acquisition with Volume Acceleration (LAVA)-flex, yielding different tissue contrasts, acquired in axial plane, and a T2-weighted MR pulse sequence with or without fat suppression, acquired in a different plane, typically coronal. Each two different MR pulse sequences per body section are acquired simultaneously with the PET scan and their acquisition time therefore not exceed the PET listening time per body section. Since the lung represents the most common site of distant metastases encountered in head and neck cancer patients, it should be addressed by a dedicated MR pulse sequence for lung tissue imaging. Such may be a motion-corrected, respiration-triggered T2-weighted MR pulse sequence using oblique k-space trajectories or periodically rotated overlapping parallel sampling (eg, PROPELLER, BLADE, MultiVane etc.), or MR sequences with ultra-short or zero time to echo. If the first type of pulse sequence is obtained, the acquisition frame may be expanded slightly in order to cover the upper abdomen as well. If gadolinium contrast medium is used for the dedicated head and neck MR scan, a second identical axial Dixon-type T1-weighted MR pulse may be acquired after contrast administration, covering the whole-body (Fig. 1).

An overview of results of recent major studies on PET/MR in head and neck cancer is provided in Table 1. In this table, if not specified otherwise, the term “head and neck cancer” alludes to various malignant neoplasms, not limited to squamous cell etiology. If no specific radiotracer is mentioned, then FDG is implied.

**T Staging**

In the local staging of primary tumor extent and infiltration of adjacent structures, the vast majority of comparative studies reports a draw between PET/MR and PET/CT. However, the median number of subjects (n = 35) in these studies is comparably low, ranging from 14 in the study by Partovi et al to 150 in the study by Kuhn et al. The latter authors compared contrast-enhanced PET/CT, T2-weighted PET/MR and contrast-enhanced T1-weighted PET/MR of the head and neck. They report slight advantages of both PET/MR techniques over PET/CT for local tumor staging, and particular advantages of contrast-enhanced T1-weighted PET/MR with regard to infiltration of neighboring structures by tumors and perineural tumor spread. Moreover, the assessment of tumors is differently affected by imaging artifacts, depending on their location: Tumors arising in the oral cavity and oropharynx are more affected by artifacts on PET/CT (mainly beam hardening artifacts from dental hardware), while tumors arising in the hypopharynx and larynx are more affected by artifacts on PET/MR (mainly motion artifacts from swallowing).

In a cohort of 35 patients with nasopharyngeal carcinoma, Cheng et al also report superiority of T2-weighted and non-enhanced T1-weighted PET/MR over PET/CT in the local tumor staging. They, however, do not provide data on contrast-enhanced PET/MR. Sekine et al specifically addressed resectability-defining factors, such as vessel encasement, prevertebral space invasion and bone invasion, and report equally favorable performance of contrast-enhanced PET/CT and PET/MR containing a fully diagnostic regional MR protocol. However, the identification of prevertebral space

![](image1.png) **Figure 1** Incidental dural metastasis identified on a whole-body PET/MR scan. While the lesion (arrow) is well seen on the axial contrast-enhanced T1-weighted fat-suppressed MR image (A, LAVA-flex), it is not as easily appreciated on the fused PET/MR image (B, arrow) because its uptake is within the range of normal cortex. Acquisition of this MR pulse sequence takes only approximately 2:30 minutes for the whole body.
| First Author, Year Published | Study Design | Number of Subjects | PET/MR System | Main Results |
|-----------------------------|-------------|--------------------|--------------|-------------|
| Covello et al, 2015<sup>17</sup> | Prospective | 44 | Biograph mMR, Siemens | High agreement on tumor ROI and PET measures among PET/MR and PET/CT. |
| Rasmussen et al, 2015<sup>100</sup> | Prospective | 30 | Biograph mMR, Siemens | FDG uptake parameters in PET/CT and PET/MR are highly reproducible. |
| Schaarschmidt et al, 2016<sup>16</sup> | Retrospective | 25 | Biograph mMR, Siemens | PET/MR and PET/CT are equal in tumor staging and recurrence detection. |
| Leibfarth et al, 2016<sup>55</sup> | Retrospective | 15 | Biograph mMR, Siemens | Multiparametric PET/MR provides substantial different functional imaging data, which may be useful for cancer treatment adaptation. |
| Surov et al, 2016<sup>88</sup> | Prospective | 11 | Biograph mMR, Siemens | DWI and PET parameters derived from PET/MR are correlated with different histopathological parameters, such as proliferation index and Ki 67 level. |
| Cavaliere et al, 2017<sup>35</sup> | Prospective | 16 | Biograph mMR, Siemens | Laryngeal carcinoma: |
| | | | | • PET/MR is useful for staging and may help treatment planning. |
| | | | | • Significant correlations of PET parameters, DWI-derived parameters and perfusion. |
| Sekine et al, 2017<sup>14</sup> | Prospective | 27 | Trimodality PET/CT+MR, GE | PET/MR and PET/CT are equal in whole-body staging of head and neck cancer. |
| Leifels et al, 2017<sup>96</sup> | Prospective | 34 | Biograph mMR, Siemens | Head and neck squamous cell carcinoma metabolism, diffusivity and perfusion depend on tumor grading. |
| Sekine et al, 2017<sup>15</sup> | Prospective | 58 | Trimodality PET/CT+MR, GE | Contrast-enhanced PET/MR and contrast-enhanced PET/CT are equal in defining local resectability of head and neck cancer. |
| Rasmussen et al, 2017<sup>58</sup> | Prospective | 21 | Biograph mMR, Siemens | Radiation therapy planning: |
| | | | | • Gross tumor volumes derived by different PET/MR techniques (T2w, FDG-PET, DWI) are similar (82% overlap). |
| | | | | • No correlation between FDG uptake and DWI. |
| Wang et al, 2017<sup>59</sup> | Prospective | 11 | Biograph mMR, Siemens | Radiation therapy planning: Gross tumor volumes derived by PET/MR and CT are similar. |
| Chan et al, 2018<sup>72</sup> | Prospective | 113 | Biograph mMR, Siemens | Nasopharyngeal carcinoma: |
| | | | | • T staging: PET/MR «more accurate» than MR in 4/113 subjects (no P value reported). |
| | | | | • N staging: Equal accuracy of PET/MR (99.3%), PET/CT (96.3%) and MR (98.2%) (P = 0.87). |
| | | | | • M staging: Similar accuracy of PET/MR (98.9%), PET/CT (97.8%) and MR (97.6%) (no P value reported). |
| Becker et al, 2018<sup>6</sup> | Prospective | 74 | Ingenuity, Philips | Recurrent head and neck cancer: |
| | | | | • PET/MR with DWI: High sensitivity (97.4%) and specificity (91.7%) for recurrence detection after radiochemotherapy. |
| | | | | • Excellent agreement between imaging-based T-stage and pathological T-stage (kappa 0.84). |
| | | | | • PET/DWI-MRI may facilitate salvage surgery planning in the irradiated neck. |
| First Author, Year Published | Study Design | Number of Subjects | PET/MR System | Main Results |
|-------------------------------|-------------|--------------------|---------------|--------------|
| Kim et al, 2018<sup>72</sup>  | Prospective | 72                 | Biograph mMR, Siemens | Combined PET/MR parameters (metabolic volume corrected by cellularity derived from ADC) may predict tumor recurrence after surgery. |
| Jentzen et al, 2018<sup>61</sup> | Prospective | 16                 | Biograph mMR, Siemens | Thyroid carcinoma: |
|                              |             |                    |               | • Neck lesion quantification with $^{124}$I-PET/MR is comparable to $^{124}$I-PET/CT for activity concentrations above 1 kBq/mL. |
| Kirchner et al, 2019<sup>68</sup> | Retrospective | 10                | Biograph mMR, Siemens | Adenoid cystic carcinoma: |
|                              |             |                    |               | • Higher diagnostic accuracy of PET/MR (91%) vs MR (84%), $P < 0.05$, for detecting locally recurrent adenoid cystic carcinoma. |
|                              |             |                    |               | • High negative predictive value of PET/MR (93%) vs MR (73%) considered particularly useful in clinical setting. |
| Samolyk-Kogaczewska et al, 2019<sup>95</sup> | Prospective | 10                | Biograph mMR, Siemens | Radiation therapy planning: 30%-40% SUV<sub>max</sub> works best for gross tumor volume delineation. |
| Olin et al, 2019<sup>98</sup>  | Retrospective | 11                | Biograph mMR, Siemens | Multiparametric PET/MR imaging analysis of head and neck cancer requires proper preparation of imaging modalities. |
| Cheng et al, 2020<sup>25</sup> | Not mentioned | 35               | Trimodality PET/CT+MR, GE | Nasopharyngeal carcinoma: |
|                              |             |                    |               | • PET/MR and PET/CT are roughly equal, with slight advantages for PET/MR in analyzing primary tumors and lymph nodes. |
|                              |             |                    |               | • No association of PET parameters, DWI-derived parameters and IVIM-derived parameters. |
| Samolyk-Kogaczewska et al, 2020<sup>29</sup> | Not mentioned | 38               | Biograph mMR, Siemens | PET/MR superior to CT in T staging and N staging. |
| Pizzuto et al, 2020<sup>32</sup> | Retrospective | 50               | Signa PET/MR, GE | Sublingual glands (not mylohyoid muscles) yield highest FDG uptake in normal floor of the mouth. |
| Dang et al, 2020<sup>97</sup>  | Prospective | 23               | Signa PET/MR, GE | Squamous cell carcinoma: Multiparametric PET/MR may allow prognosticating tumor grading. |
| Klain et al, 2020<sup>74</sup> | Prospective | 40               | Biograph mMR, Siemens | Thyroid carcinoma: |
|                              |             |                    |               | • PET/MR and PET/CT are equal in following-up patients with elevated serum thyroglobulin levels after thyroidectomy and radioiodine therapy. |
| Huang et al, 2020<sup>26</sup> | Prospective | 20               | Signa PET/MR, GE | Hypopharyngeal carcinoma: |
|                              |             |                    |               | • T staging: Equal accuracy of PET/MR (81.6%), PET/CT (63.6%) and MR (72.7%). |
| Park et al, 2020<sup>36</sup>  | Retrospective | 73               | Biograph mMR, Siemens | PET/MR is superior to MR and PET alone in lesion classification in head and neck cancer. |

If no radiotracer is stated for a given study, FDG is implied.
invasion and the differentiation of local tumor recurrence and postradiogenic osteonecrosis remains a challenging task for cross-sectional hybrid imaging, even if intravenous contrast is used.\textsuperscript{27,28}

Most available PET/MR studies discuss rather heterogeneous cohorts of squamous cell carcinoma arising in the head and neck, and some studies include non-squamous cell malignancies as well. Data on specific tumor subsites in the head and neck is scarce, as well as specific data on non-squamous cell tumors. Also, some PET/MR studies lack comparative data on PET/CT, which still serves as a standard of reference for oncological cross-sectional hybrid imaging. Samodzik-Kogaczewska et al report superiority of PET/MR over CT imaging in the primary tumor staging of a cohort of mainly moderately differentiated (G2) squamous cell carcinomas of various origins.\textsuperscript{29} In a large prospective study on nasopharyngeal carcinoma patients, Chan et al reported PET/MR to be "more accurate" than MR in 4 out of 113 subjects, however, without providing a $P$ value.\textsuperscript{22} Huang et al recently reported in 20 patients with hypopharyngeal carcinoma that PET/MR performs equally well as PET/CT and MR, with insignificant advantages for PET/MR (diagnostic accuracy: \textsuperscript{26}PET/MR 81.6%, PET/CT 63.6%, MR 72.7%). In a small cohort of oral and oropharyngeal carcinoma patients (n = 11), all with histopathological standard of reference, Hayashi et al reported that separately acquired and retrospectively fused PET-MR images facilitate the assessment of mandible and medial pterygoid infiltration, both of which rendering such a tumor either T4 (p16-positive) or T4a (p16-negative).\textsuperscript{30} They also report that PET-MR is easy to understand for non-radiologists, such as head and neck surgeons. However, retrospectively fused PET-MR images are known to have inferior registration accuracy compared to simultaneously acquired PET/MR image datasets in head and neck cancer patients.\textsuperscript{31} Cavaliere et al in their study on 16 patients with laryngeal carcinoma report that PET/MR has "relevant clinical impact", mainly by assisting in treatment planning (9 of 16 subjects). Endoscopic findings were confirmed in 6 of 16 subjects, while the endoscopic staging of the primary tumor was modified only in one single subject.

The local assessment of head and neck tumors may be challenged by structures that physiologically exhibit 18F-fluorodeoxyglucose (FDG) uptake, such as muscles or salivary glands, and which may be closely related and exhibit similar density on CT. A recent study by Pizzuto et al using PET/MR confirmed that it is in fact the sublingual glands that show physiological high FDG uptake in the floor of the mouth, and not the mylohyoid muscles.\textsuperscript{32-34}

\textbf{Figure 2} Perineural spread in PET/MR (contrast-enhanced T1-weighted fat-suppressed images). FDG-avid contrast-enhancing tumor extension is seen along the trigeminal nerve in the lateral wall of the cavernous sinus and in Meckel’s cave (arrows on A and B), all the way to the thickened cisternal segment of the nerve and the root entry zone in the pons (arrowhead on A and B).

\textbf{Figure 3} Perineural spread in PET/MR (same subject as in Fig. 2). FDG-avid tumor extension is seen within and below the foramen ovale along the mandibular nerve (arrow), which is the largest of the three major branches of the trigeminal nerve, and further behind the condylar neck of the mandible along the auriculotemporal nerve (arrowheads), which is the posterior and larger division of the mandibular nerve.
Perineural tumor extension refers to tumor growth along nerves and accompanying structures, in the head and neck mainly occurring along larger cranial nerves and their branches, sometimes unto the brain stem (Fig. 2). While the majority of adenoid cystic carcinomas exhibit such perineural spread, owing to their overall greater incidence, it is mainly seen with run-of-the-mill squamous cell carcinomas (Fig. 3). The presence of perineural spread implies a bad prognosis for patients, and may change or preclude a surgical approach and impact on the radiation therapy volume. Nevertheless, it is often overlooked, even in clinically symptomatic patients. Its detection therefore warrants scrutinizing of images. PET/MR generally is believed to surpass both MR and PET/CT in the assessment of perineural spread. However, so far, only a few studies reported on this topic. Kuhn et al state that perineural spread in their cohort of 150 patients with mainly T2 to T4 tumors was detected overall in 7% of subjects with PET, in 2% with MR, and in 1% with CT. They, however, do not provide a direct comparison of PET/MR and PET/CT. Such was done in a study by Sekine et al, who reported perineural spread in 22% of locally advanced squamous cell carcinomas. Here, PET/MR and PET/CT reach equal high accuracy (100% vs 98%, respectively).

N Staging

As with T staging, the majority of PET/MR studies covers mainly unselected cohorts of head and neck cancers. An overall equal performance in comparison with PET/CT is reported. In nasopharyngeal carcinoma, Chan et al report an equal diagnostic accuracy of PET/MR (99.3%), PET/CT (96.3%), and MR (98.2%) (P = 0.87). In the same tumor entity, Cheng et al report a slight advantage of T2-weighted PET/MR imaging over T1-weighted PET/MR imaging in nodal staging (Fig. 4). Also in the nodal staging of hypopharyngeal carcinoma, a tumor entity that frequently exhibits regional lymph node metastases, evidence exists that PET/MR reaches equal sensitivity and specificity as PET/CT and MR. In their study on laryngeal carcinomas, Cavaliere et al do not comment on the N staging, probably owing to the small cohort of only 3 nodal positive subjects out of a total of 16. The larynx, particularly the glottic area with the true vocal cords, is known for its paucity of lymphatics. Not surprisingly, the studies by Park et al and Samošyk-Kogaczewska et al report superior performance of PET/MR compared to MR alone and CT alone in cohorts of squamous cell carcinomas of various origins. In their large general head and neck cancer cohort, Kuhn et al claimed that PET/MR without contrast, which in their study performed equally well as contrast-enhanced PET/CT, might hence easily replace PET/CT in patients who cannot receive contrast medium.

M Staging and Second Primary Tumors

Data is somewhat scarce concerning the M staging and the detection of second primary tumors in patients with head and neck cancer that underwent PET/MR. This finding might be due to the overall comparably low median number of study subjects on the one hand, and due to the only approximately 5%-10% of head and neck cancer patients exhibiting distant metastases or second primary tumors at their initial staging on the other hand. Within one year, approximately 10% of head and neck cancer patients develop metastatic distant metastases, increasing to approximately 20% by 5 years. Approximately two thirds of distant metastases occur in the lung, followed by the bone and liver, if cervical soft tissue metastases are excluded. While the lung initially was considered problematic for PET/MR, in oncological populations it actually turned out to work well. Dedicated MR pulse sequences for lung imaging used in PET/MR can detect nodules of only 3 mm size on the one hand, while on the other hand nodules...
missed on PET/MR do not grow in 97%, and FDG-negative sub-centimeter nodules are benign in >98%. Novel MR pulse sequence with zero time to echo (ZTE) are becoming available in PET/MR and show promising results for the assessment of lung parenchyma.

A large recent meta-analysis covering more than 450,000 head and neck cancer patients showed that 5% of patients have synchronous second primary tumors, and 13% of patients will have metachronous primary tumors within 2 years’ time. The majority of second primary tumors occur in the upper aerodigestive tract, followed by the lung. Hence, PET/MR might prove valuable in the detection of distant metastases and second primary tumors. Sekine et al had only one single patient with distant metastasis in their cohort of patients referred for initial staging. Partovi et al had a total of 38 distant metastases in their cohort of 14 patients referred mainly for restaging, and report a similar performance of PET/MR and PET/CT in assessing these lesions, but do not specifically comment on staging. Chan et al report similar diagnostic accuracy of PET/MR (98.9%), PET/CT (97.8%), and MR (97.6%) in 113 nasopharyngeal carcinoma patients with a total of 30 distant metastases. Specific PET/MR data on second primaries in head and neck cancer patients is currently lacking. There is, however, evidence that PET/MR might surpass PET/CT in the detection of hitherto occult primaries particularly in the head and neck region, indicating that PET/MR might also perform well in the incidental detection of second primaries.

Radiation Therapy Planning

PET-based radiation therapy planning offers several advantages over conventional morphological radiation therapy planning in head and neck cancer patients. The probably most important advantage lies in the more holistic identification of disease extent — not only in the head and neck region but also with regard to distant sites. Using FDG as radiotracer, PET-based radiation therapy planning reduces the risk of geographical miss of radiation delivery to the gross tumor volume in head and neck cancers. The use of other radiotracers, such as 18F-fluoromisonidazole (F-MISO) or 18F-fluorooazomycin (FAZA) that serve as biomarkers for hypoxia, may characterize the biological behavior of tumors, identifying tissues that deserve modulated or escalated radiation therapy approaches. Other biomarkers important for radiation therapy planning may also be derived from MR imaging, such as the vascularity and permeability of tissues using perfusion-weighted imaging (PWI) or the cellularity using diffusion-weighted imaging (DWI). Increasing attention has been paid in the last years to MR-guided radiation therapy systems, which can image and treat cancer patients simultaneously, and first technical studies have recently been published showing the feasibility in head and neck cancer patients. For these reasons, PET/MR-based radiation therapy planning appears to be an appealing option in head and neck cancer patients.

However, data on PET/MR-based radiation therapy planning is somewhat scarce. Three prospective studies targeted this topic, with results in radiation therapy planning available in 10-12 patients per study, all examined with FDG. Rasmussen et al examined different PET/MR-derived tumor delineation techniques (T2w, FDG-PET, DWI) and reported a similar performance of methods, with 82% overlap of gross tumor volumes. Wang et al state that PET/MR-derived gross tumor volumes also match CT-derived gross tumor volumes, achieving similar radiation doses. Samołyk-Kogaczewska et al focused on which volume threshold of the maximum standardized uptake value (SUVmax) serves best for primary tumor delineation and nodal gross tumor volume, reporting best results for 30% SUVmax and 30-40% SUVmax, respectively. PET/MR-based radiation therapy planning of the head and neck region in clinical routine requires positioning devices, such as masks and a flat tabletop for the PET/MR gantry, which impedes with the rather narrow gantry gauge of PET/MR scanners. The latter represents still an unsolved issue, limiting the clinical usage of PET/MR for radiation therapy planning of head and neck cancer.

For radioiodine therapy planning, Jentzen et al showed that neck lesion quantification with 124I-PET/MR is comparable to 124I-PET/CT for activity concentrations above 1 kBq/mL. Hence, PET/MR may be used for pre-therapy dosimetry painting in patients with differentiated thyroid carcinoma.

Treatment Response Assessment and Recurrence Detection

The detection of tumor persistence or recurrence within tissues altered by surgery and/or radiotherapy is a challenging task, both for clinicians and for radiologists. Owing to the high intrinsic soft tissue contrast, MR is superior to CT for this task. PET/CT in the other hand is believed to be superior to both CT and MR, mainly owing to its high negative predictive value, although familiarity with false-positive findings, such as postradiographic inflammation or muscle tonicity, is required. PET/MR, combining the aforementioned advantages of PET and MR, hence may represent an optimal approach to tackle this issue.

Queiroz et al in their study on 87 patients found that PET/MR and PET/CT overall perform equally well in local recurrence detection, but explicitly mention that PET/MR specifies focal FDG uptake better than PET/CT, thereby decreasing false-positive results. Both Sekine et al and Schaarschmidt et al also report similar performance of both modalities in the restaging of head and neck cancer patients. Becker et al in 74 patient with recurrent head and neck cancer report high sensitivity (97%) and specificity (92%) for recurrence detection after radiochemotherapy using PET/MR including DWI, and an excellent agreement between the T stage
derived by PET/MR imaging and the one derived by pathol-
ygy (kappa 0.84).56

In a small but selected cohort of patients (n = 10, with a
total of 32 examinations) with locally recurrent adenoid
cystic carcinoma, Kirchner et al reported higher diagnostic accu-
racy of PET/MR compared to MR (91% vs 84%,
respectively). They claimed that particularly the high nega-
tive predictive value of PET/MR compared to MR (90% vs
73%, respectively) may be beneficial in clinical routine. This
finding is not surprising, since adenoid cystic carcinoma usu-
ally exhibits comparably low but visible FDG uptake on the
one hand and frequently comes with small regional lymph
node metastases on the other hand.50-52 Hence, PET/MR
may be an optimal approach in this setting. The authors,
however, did not address extracervical recurrence, and ade-
noid cystic carcinoma is notorious for developing slowly
growing lung metastases within 2-5 years' time. Hence, a
side-by-side comparison with PET/CT would be desirable to
properly assess the value of PET/MR for this type of tumor.

In a prospective study analyzing 72 patients before treat-
ment, Kim et al identified several PET/MR-derived bio-
markers as predictors of recurrence after surgery, among
them the metabolic tumor volume, the ratio of metabolic
tumor volume and mean apparent diffusion coefficient
(ADC\text{mean}), and the ratio of total lesion glycolysis and
ADC\text{mean}.53 Another recent study used retrospective PET-MR
fusion and found combined FDG-PET/MR parameters
(volumes derived from DWI and FDG-PET) to predict
clinical outcome in rhabdomyosarcoma patients.54 Hence,
combined PET/MR parameters may have prognostic capabil-
ity in head and neck cancer patients.

**Thyroid cancer, orphan tumors, and non-FDG radiotracers**

FDG-PET/CT represents the most accurate imaging modality
in the staging and restaging of patients with differentiated
thyroid carcinoma of an aggressive histology, with radioio-
dine-negative malignant lesions, or in patients with increased
thyroglobulin serum concentration in the absence of patho-
logic imaging findings.55 A recent study by Klain et al in 40
patients proved equal performance of PET/MR and PET/CT
in following-up 40 subjects with differentiated thyroid cancer
and elevated thyroglobulin levels.56 Jentzen et al covered the
potential of pre-therapeutic dosimetry painting in patients
with differentiated thyroid carcinoma using 124I-PET/MR
(for details, please see above).60

Specific PET/MR studies on major salivary gland tumors
are currently lacking. It is expected that PET/MR might be
useful for the work-up of such lesions, owing to the large
variety of tumor entities arising in this location and their het-
erogeneous MR signal characteristics and uptake characteris-
tics (Fig. 5).

Pourmehdi Lahiji et al reported that the overlap of hyper-
metabolism plus restricted diffusion predict unfavorable out-
come in pediatric and adolescent patients with
rhabdomyosarcoma of the neck.57 These authors, however,
used separately acquired PET and MR image datasets that
were retrospectively fused by software. To date, no data on
PET/MR using FDG, DOTA-peptides or 18F-dihydroxyphe-
nylalanine in paragangliomas of the head and neck exist.
However, a single case of a retroperitoneal pheochromocyt-
toma imaged with FDG-PET/MR was reported in a study on
succinate dehydrogenase mutation-related pediatric pheo-
chromocytomas and paragangliomas.58 The generally lower
radiation exposure with PET/MR compared to PET/CT is
another indisputable advantage, particularly in the pediatric
and adolescent population.

A favorable performance of 18F-choline PET/MR has been
reported in patients with primary hyperparathyroidism and
hitherto occult parathyroid adenomas or hyperplasias.59-61
No data currently exists on 18F-choline PET/MR in parathy-
roid malignancies (Fig. 6).

**Technical Issues**

**Motion Correction in PET/MR in Head and
Neck Cancer Patients**

In head and neck cancers patients, motion affects image qual-
ity most often in two ways: First, repetitive, predictable and
unidimensional movement of the chest and upper abdomen
due to respiration, and second, non-repetitive, unpredictable
and multidimensional bulk movement in the head and neck.
Both types of motion impact on PET and MR data.

Since the lung represents an important distant site in head
and neck cancer patients with regard to metastases and

![Figure 5](image_url)

**Figure 5** Acinic cell carcinoma of the parotid gland. The well-defined tumor (arrow) is T2w-hyperintense (A), enhances
only little contrast medium if any (B) and is FDG-negative (C).
second primary tumors, a proper consideration of motion is
desired here. Since the acquisition of images covering the
whole chest (approximately 6 minutes) exceeds patients’
breathhold capability, all clinical MR pulse sequences for
lung imaging (eg, T2-weighted propeller, ZTE) use gating
devices that recognize the respiratory cycle and allow image
acquisition during the quiescent phase.\textsuperscript{9,10,42,45} Such devices
are typically external ones placed on the patient, such as bel-
lows, but image-based tracking has been used as well.\textsuperscript{18,79,80}
External gating devices have also been used for motion cor-
rection of PET, either bellows or reflecting markers and infra-
red cameras. Beyond being time consuming and somewhat
uncomfortable for patients, this technique has several draw-
backs. Most importantly, motion can only be corrected for in
one single bed position, which must be prescribed before the
scan. Also, technical failure may spoil the whole acquisition.
In recent years, novel deviceless gating techniques were
developed that rely solely on PET data.\textsuperscript{81,82} These techniques
outperform external gating methods.\textsuperscript{81} In brief, PET coinci-
dence data is broken down into dynamic sinograms. A prin-
cipal component analyses then decomposes these sinograms
into a set of components with the maximum variation in data
over time. Finally, a Fourier transformation of these compo-
nents identifies respiratory motion, generating waveforms
and triggers. If significant motion is detected, it is automati-
cally corrected.\textsuperscript{82} This software-based method today is only
available with PET/CT scanners, but is expected to be imple-
mented in PET/MR scanners as well.

Things are more complicated with bulk motion of the
head and neck, which is typically nonrepetitive, unpredict-
able and may occur in more than one direction. Software-
based solutions for PET are expected to solve this problem in
the future.\textsuperscript{84,85} Unlike PET, MR acquisition is typically
repeated if it is spoiled by bulk motion, but correction meth-
ods exist as well.\textsuperscript{84} The combination of PET and MR bulk
motion correction techniques might amend the known swal-
lowing-related shortcomings of PET/MR compared to PET/
CT that are encountered in the larynx and hypopharynx.\textsuperscript{24}

**Dental Artifacts**

Artifacts elicited by dentures and other metallic dental work
are known to impact on PET/MR image quality, both by dist-
torting the MR-based attenuation correction of PET emission
data, and by spoiling MR image quality. Ladefoged et al
showed in 148 PET/MR patients that dental hardware leads
to severe MR signal voids, and that the resulting PET/MR arti-
facts exceed the volume of dental hardware.\textsuperscript{86} This causes
severe bias in PET data in and near to the signal voids, affect-
ing the conspicuity of lesions in the jawbone.\textsuperscript{86} Gunzinger et
al in a study with 25 subjects have shown that MR pulse
sequences with multiacquisition variable-resonance image
combination might be useful for the reduction of artifacts eli-
cited by dental implants in PET/MR, potentially improving
the diagnostic accuracy in patients with oral and oropharyn-
geal carcinoma.\textsuperscript{87}

**MR-based Attenuation Correction in the
Head and Neck**

In the same study, Gunzinger et al have also shown that
relative errors in SUV calculation through MR-based atten-
uation correction are negligible for simulated artifacts of
0.5 cm size, but become substantial (relative error -33%) if
the artifact size is increased to 5.2 cm.\textsuperscript{87} Ladefoged et al
report an MR-based volume of susceptibility-induced sig-
nal voids on the MR-AC attenuation maps to range
between 1.6 and 520.8 mL.\textsuperscript{86} They also report significant
underestimation of SUV that is correlated with the volume of
the susceptibility artifact on the MR attenuation map,
decreasing with the distance to the signal void.\textsuperscript{86} Both of
these studies used Dixon-type MR pulse sequences for
MR-based attenuation correction. Wiesinger et al used
ZTE-based pseudo-CT image conversion in the whole
head for this purpose.\textsuperscript{88} They report this method to be
accurate, robust and fast.\textsuperscript{88}
PET Image Reconstruction Techniques

A novel PET image reconstruction technique relies on a Bayesian penalized likelihood reconstruction algorithm (block sequential regularized expectation maximization [BSREM]).\textsuperscript{90,91} It yields reportedly higher signal-to-noise ratio and higher SUV compared to conventional ordered subset expectation maximization in mediastinal lymph node assessment, but does not improve the accuracy of N staging.\textsuperscript{91} Another study showed that artificial intelligence using deep learning yields better results in lung nodule assessment with BSREM compared to ordered subset expectation maximization.\textsuperscript{92} While BSREM is used on many digital PET/CT scanners, it is also increasingly available on PET/MR scanners.\textsuperscript{93} To date, no results have been published concerning the use of BSREM in PET/MR in head and neck cancer patients.

Functional MR Techniques and Multiparametric PET/MR

In a clinical setting, Queiroz et al have shown that the addition of DWI does not provide additional value for the staging of 70 head and neck cancer patients with PET/MR, while Becker et al pointed out that DWI might be particularly useful to detect local tumor recurrence.\textsuperscript{70,71} Most research questions about multiparametric PET/MR using different functional MR techniques in conjunction with PET revolve around the additive value of such techniques and their use as surrogate markers — alone or in combination — for different endpoints, such as biological characteristics and behavior of tumor, its responsiveness to therapy, as well as the disease-specific survival of patients. Hitherto published PET/MR studies in head and neck cancer cover DWI, perfusion-weighted imaging and intravoxel incoherent motion. These studies report different and partly contradicting results.\textsuperscript{5,6} Varoquaux et al and Leibfarth et al found no association of PET parameters and DWI-derived parameters in primary tumors; both techniques might therefore be complementary.\textsuperscript{94,95} Leifels et al reported different correlations of PET parameters with DWI parameters and PWI parameters in 34 patients with head and neck cancer, which are related to tumor grading.\textsuperscript{96} Dang et al reported a correlation of PET parameters with PWI parameters, but not with DWI parameters in 23 patients, stating multiparametric PET/MR might predict tumor grading.\textsuperscript{97} Surov et al in a study with 11 subjects stated that primary tumor PET parameters and DWI parameters from PET/MR are correlated with different histopathological parameters, such as the proliferation index and the Ki 67 level.\textsuperscript{98} Kim et al reported that a combination of PET parameters and ADC may predict treatment failure (see above).\textsuperscript{12}

Caution is warranted when interpreting the results of these studies. Beyond the rather small median number of subjects which might limit the significance of results, comparability of data might also be affected by the lack of inter-scanner harmonization, different acquisition and reconstruction techniques, and different preparation methods or the omission of such. Olin et al showed that incorporating point spread function modelling into PET image reconstruction affects tumor quantification (10%-20% increase in SUV).\textsuperscript{99} DWI geometric distortion can be reduced by correction methods. Both parameters sets are influenced differently: While the PET reconstruction technique (point spread function) has little influence on spatial correlation with DWI, distortion correction of DWI significantly affects the spatial correlation with PET.\textsuperscript{70} Hence, in order to properly conduct, analyze and interpret multiparametric PET/MR studies of head and neck cancer, an appropriate preparation of the imaging modalities is essential.\textsuperscript{99}

Summary

PET/MR is a valid and clinically accepted imaging tool in the head and neck. Overall, it provides at least equal diagnostic accuracy as PET/CT, offering advantages over PET/CT in specific clinical situations, besides the generally lower radiation burden. In the future, specific PET/MR studies are desired addressing specific histopathological tumor entities and specific anatomical subsites in the head and neck, as well as malignancies imaged with non-FDG radiotracers.

Acknowledgment

The author of this review article is indebted to (in alphabetical order): Panagiotis Balermpas MD, Felipe Barbosa MD, Marta Bogowicz PhD, Martina Broglie D"{u}ppen MD, Irene Burger MD, Hugh Curtin MD PhD, Gaspar Delso PhD, Sabrina Epp, Thomas Gander MD, Helena Garcia Sch"{u}ler MD, Hannes Gr"{u}ning MD, Marlena Hofbauer, David Holzmann MD, Gerhard Huber MD, Lars Husmann MD, Kristian Ikenberg MD, Philipp Kaufmann MD, Freya Klein, Spyros Kollias MD, Fotis Kotasis PhD, Felix Kuhn MD, MD, Virginia Liberini MD, C"{a}cilia Mader MD, Alexander Maurer MD, Christian Meerwein MD, Michael Messerli MD, Gr"{e}goire Morand MD, Erika Orita MD PhD, Daniele Pizzuto MD, Marcelo Queiroz MD, Tamara Rordorf MD, Niels Rupp MD, Christoph Schmid MD, Stefan Schmid MD, Bernhard Schuknecht MD, Paul Schumann MD, Tetsumu Sekine MD PhD, Jakub Siennicki PhD, Bernd Stadlinger, MD, Paul Stolzmann MD, Klaus Strobel MD, Edwin ter Voert, PhD, Thomas Treumann MD, Valerie Treyer PhD, Josephine Trinckauf, Patrick Veit-Haibach MD, Domenic Vital MD, Gustav von Schulthess MD PhD, Verena Weichselbaumer, Michael Wissmeyer MD, Robert Witte MD PhD.

References

1. von Schulthess GK, Kuhn FP, Kaufmann P, et al: Clinical positron emission tomography/magnetic resonance imaging applications. Semin Nucl Med 43:3-10, 2013
2. Queiroz MA, Huellner MW: PET/MR in cancers of the head and neck. Semin Nucl Med 45:248-265, 2015
PET/MR in Head and Neck Cancer – An Update

45. Stolzmann P, Veit-Halbach P, Chuck N, et al: Detection rate, location, and size of pulmonary nodules in trimalaritrost PET/CT-MR. Comparison of low-dose CT and Dixon-based MR imaging. Invest Radiol 48:241-246, 2013

46. Raad RA, Friedman KP, Heacock L, et al: Outcome of small lung nodules missed on hybrid PET/MRI in patients with primary malignancy. J Magn Reson Imaging 43:504-513, 2016

47. Chang ST, Nguyen DC, Raptis C, et al: Natural history of preoperative subcentimeter pulmonary nodules in patients with resectable pancreatic adenocarcinoma: A retrospective cohort study. Ann Surg 261:970-975, 2015

48. Sekine T, Barbosa FG, Sah BR, et al: PET/MR outperforms PET/CT in suspected occult tumors. Clin Nucl Med 42:e88-e95, 2017

49. Ruhlmann V, Ruhlmann M, Bellendorf A, et al: Hybrid imaging for detection of carcinoma of unknown primary: A preliminary comparison trial of whole-body PET/MRI versus PET/CT. Eur J Radiol 85:1941-1947, 2016

50. Arslan S, Abakay CD, Sen F, et al: Role of PET/CT in treatment planning for head and neck cancer patients undergoing definitive radiotherapy. Asian Pac J Cancer Prev 15:10899-10903, 2014

51. Meola RN, Kayani I, Mominuddin SA, et al: The potential advantages of (18)FDG PET/CT-based target volume delineation in radiotherapy planning of head and neck cancer. Radiother Oncol 97:189-193, 2010

52. Newbold K, Powell C. PET/CT in radiotherapy planning for head and neck cancer. Front Oncol 2:189, 2012

53. Minn H, Suiolamo S, Seppala J. Impact of PET/CT on planning of radiotherapy in head and neck cancer. Q J Nucl Med Mol Imaging 54:521-532, 2010

54. Bollineni VR, Koole MJ, Pruim J, et al: Dynamics of tumor hypoxia assessed by 18F-FAZA PET/CT in head and neck and lung cancer patients during chemoradiation. Possible implications for radiotherapy treatment planning strategies. Radiother Oncol 113:198-203, 2014

55. Greigore V, Guckenberger M, Haustermans K, et al: Image guidance in radiation therapy for better cure of cancer. Mol Oncol 14:1470-1491, 2020

56. Ng-Cheng-Hin B, Nutting C, Newbold K, et al: The impact of restricted length of treatment field and anthropometric factors on selection of head and neck cancer patients for treatment on the MR-Linac. Br J Radiol 93:20200023, 2020

57. Chuter RW, Pollitt A, Whitehurst P, et al: Assessing MR-linac radiotherapy robustness for anatomical changes in head and neck cancer. Phys Med Biol 63:125020, 2018

58. Rasmussen JH, Norgaard M, Hansen AE, et al: Feasibility of multiparametric imaging with PET/MR in head and neck squamous cell carcinoma. J Nucl Med 58:69-74, 2017

59. Wang K, Mullins BT, Falchook AD, et al: Evaluation of PET/MRI for tumor volume delineation for head and neck cancer. Front Oncol 7:8, 2017

60. Samolyk-Kogaczewska N, Sierko E, Zuzda K, et al: PET/MR-guided GTV delineation during radiotherapy planning in patients with squamous cell carcinoma of the tongue. Strahlenther Onkol 195:780-791, 2019

61. Jenzen W, Phaorocharoen J, Gomez B, et al: Quantitative performance of (124)I PET/MR of neck lesions in thyroid cancer patients using (124)I PET/CT as reference. EJNMMI Phys 5:13, 2018

62. Saito N, Nakajbn RN, Nakabira M, et al: Posttreatment CT and MR imaging in head and neck cancer: What the radiologist needs to know. Radiographics 32:1261-1282, 2012. discussion 82-4

63. Lell M, Baum U, Greess H, et al: Head and neck tumors: Imaging recurrent tumor and post-therapeutic changes with CT and MRI. Eur J Radiol 33:239-247, 2000

64. Meerwein CM, Quenouz M, Kollaz S, et al: Post-treatment surveillance of head and neck cancer: pitfalls in the interpretation of FDG PET/CT- MRI. Swiss Med Wkly 145:w14116, 2015

65. Cheung PK, Chin RV, Estick GD: Detecting residual/recurrent head neck squamous cell carcinomas using PET or PET/CT. Systematic review and meta-analysis. Otolaryngol Head Neck Surg 154:421-432, 2016

66. Kubota K, Yokoyama J, Yamaguchi K, et al: FDG-PET delayed imaging for the detection of head and neck cancer recurrence after radio-chemotherapy. Comparison with MRI/CT. Eur J Nucl Med Mol Imaging 31:590-595, 2004

67. Varoquaux A, Rager O, Dulguerov P, et al: Diffusion-weighted and PET/MR imaging after radiation therapy for malignant head and neck tumors. Radiographics 35:1502-1527, 2015

68. Kirchner J, Schaarschmidt BM, Sauerwein W, et al: (18)F-FDG PET/ MRI vs MRI in patients with recurrent adenoid cystic carcinoma. Head Neck 41:170-176, 2019

69. Jeong HS, Chung MK, Son YI, et al: Role of 18F-FDG PET/CT in management of high-grade salivary gland malignancies. J Nucl Med 48:1237-1244, 2007

70. Roh JL, Ryu CH, Choi SH, et al: Clinical utility of 18F-FDG PET for patients with salivary gland malignancies. J Nucl Med 48:240-246, 2007

71. Park MJ, Oh JS, Roh JL, et al: 18F-FDG PET/CT versus contrast-enhanced CT for staging and prognostic prediction in patients with salivary gland cancers. Clin Nucl Med 42.e149-e56, 2017

72. Kim YI, Cheon GJ, Kang SY, et al: Prognostic value of simultaneous (18)F-FDG PET/MRI using a combination of metabolo-volumetric parameters and apparent diffusion coefficient in treated head and neck cancer. EJNMMI Res 9:2, 2018

73. Pourmehdi Lahiji A, Jackson T, Nejadnik H, et al: Association of tumor volume with (18)F[FDG activity and diffusion restriction with clinical outcomes of rhabdomyosarcomas. Mol Imaging Biol MIB Off Publ Acad Mol Imaging 21:591-598, 2019

74. Klaia M, Nappi C, Nicolai E, et al: Comparison of simultaneous (18)F-2-[18F] FDG PET/MR and PET/CT in the follow-up of patients with differentiated thyroid cancer. Eur J Nucl Med Mol Imaging 2020. https://pubmed.ncbi.nlm.nih.gov/32601803/

75. Jha A, Ling A, Millo C, et al: Superiority of (68)Ga-DOTATATE over (18)F-FDG and anatomic imaging in the detection of succinate dehydrogenase mutation (SDHx-)related phaeochromocytoma and paraganglioma in the pediatric population. Eur J Nucl Med Mol Imaging 45:787-797, 2018

76. Ahlbari AA, Alshehi FM, Albaray AA, et al: [(18)F]Fluorocholine uptake of parathyroid adenoma is correlated with parathyroid hormone level Imaging Mol Biol Off Publ Acad Mol Imaging 20:857-867, 2018

77. Huelner MW, Aberle S, Sah BR, et al: Visualization of parathyroid hyperplasia using 18F-fluorocholine PET/CT in a patient with secondary hyperparathyroidism. Clin Nucl Med 41:e139-e161, 2016

78. Kluifhou WP, Pasternak JD, Gosnell JE, et al: (18)F fluorocholine PET/MR imaging in patients with primary hyperparathyroidism and inconclusive conventional imaging: A prospective pilot study. Radiol 284:460-467, 2017

79. White N, Roddey C, Shankaranarayana A, et al: PROMO: Real-time prospective motion correction in MRI using image-based tracking. Magn Reson Med 63:91-105, 2010

80. Cet P, Serra G, Bertolo S, et al: Assessment of CF lung disease using motion corrected PROPELLER MRI. A comparison with CT. Eur Radiol 26:780-787, 2016

81. Walker MD, Morgan AJ, Bradley KM, et al: Data driven respiratory gating outperforms device-based gating for clinical FDG PET/CT. J Nucl Med 2020. https://pubmed.ncbi.nlm.nih.gov/32245898/

82. Walker MD, Bradley KM, McGowan DR. Evaluation of principal component analysis-based data-driven respiratory gating for positron emission tomography. Br J Radiol 91:20170793, 2018

83. Walker MD, Morgan AJ, Bradley KM, et al: Evaluation of data-driven respiratory gating waveforms for clinical PET imaging. EJNMMI Res 9:1, 2019

84. Kolbitsch C, Prieto C, Tsompas C, et al: A 3D MR-acquisition scheme for non-rigid bulk motion correction in simultaneous PET-MR. EJNMMI Phys 1(Suppl 1):A37, 2014

85. Sun T, Petbin Y, Han PK, et al: Body motion detection and correction in cardiac PET. Phantom and human studies. Med Phys 46:4898-4906, 2019

86. Ladelogel CN, Hansen AE, Keller SH, et al: Dental artifacts in the head and neck region: Implications for Dixon-based attenuation correction in PET/MR. EJNMMI Phys 2:8, 2015

87. Gunzinger JM, Delso G, Boss A, et al: Metal artifact reduction in patients with dental implants using multispectral three-dimensional data acquisition for hybrid PET/MRI. EJNMMI Phys 1:102, 2014
88. Wiesinger F, Bylund M, Yang J, et al: Zero TE-based pseudo-CT image conversion in the head and its application in PET/MR attenuation correction and MR-guided radiation therapy planning. Magn Reson Med 80:1440-1451, 2018
89. Messerli M, Stolzmann P, Egger-Sigg M, et al: Impact of a Bayesian penalized likelihood reconstruction algorithm on image quality in novel digital PET/CT: Clinical implications for the assessment of lung tumors. EJNMMI Phys 5:27, 2018
90. Teoh EJ, McGowan DR, Macpherson BE, et al: Phantom and clinical evaluation of the bayesian penalized likelihood reconstruction algorithm Q.Clear on an LYSO PET/CT system. J Nucl Med 56:1447-1452, 2015
91. Teoh EJ, McGowan DR, Bradley KM, et al: 18F-FDG PET/CT assessment of histopathologically confirmed mediastinal lymph nodes in non-small cell lung cancer using a penalised likelihood reconstruction. Eur Radiol 26:4098-4106, 2016
92. Schwyzer M, Martini K, Benz DC, et al: Artificial intelligence for detecting small FDG-positive lung nodules in digital PET/CT: impact of image reconstructions on diagnostic performance. Eur Radiol 30:2031-4 0, 2020
93. Ter Voert E, Muehlematter UJ, Delso G, et al: Quantitative performance and optimal regularization parameter in block sequential regularized expectation maximization reconstructions in clinical (68)Ga-PSMA PET/MRI. EJNMMI Res 8:70, 2018
94. Varoquaux A, Rager O, Lovblad KO, et al: Functional imaging of head and neck squamous cell carcinoma with diffusion-weighted MRI and FDG PET/CT: Quantitative analysis of ADC and SUV. Eur J Nucl Med Mol Imaging 40:842-852, 2013
95. Leibarth S, Simoncic U, Monnich D, et al: Analysis of pairwise correlations in multi-parametric PET/MR data for biological tumor characterization and treatment individualization strategies. Eur J Nucl Med Mol Imaging 43:1199-1208, 2016
96. Leifels L, Purz S, Stumpp P, et al: Associations between (18)F-FDG-PET, DWI, and DCE parameters in patients with head and neck squamous cell carcinoma depend on tumor grading. Contrast Media Mol Imaging 2017:5369625, 2017
97. Dang H, Chen Y, Zhang Z, et al: Application of integrated positron emission tomography/magnetic resonance imaging in evaluating the prognostic factors of head and neck squamous cell carcinoma with positron emission tomography, diffusion-weighted imaging, dynamic contrast enhancement and combined model. Dentomaxillofac Radiol 49:20190488, 2020
98. Surov A, Stumpp P, Meyer HJ, et al: Simultaneous (18)F-FDG-PET/MRI: Associations between diffusion, glucose metabolism and histopathological parameters in patients with head and neck squamous cell carcinoma. Oral Oncol 58:14-20, 2016
99. Olin A, Krogager L, Rasmussen JH, et al: Preparing data for multiparametric PET/MR imaging. Influence of PET point spread function modelling and EPI distortion correction on the spatial correlation of [(18)F]FDG-PET and diffusion-weighted MRI in head and neck cancer. Phys Med 61:1-7, 2019
100. Rasmussen JH, Fischer BM, Aznar MC, et al: Reproducibility of (18)F-FDG PET uptake measurements in head and neck squamous cell carcinoma on both PET/CT and PET/MR. Br J Radiol 88:20140655, 2015