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Does extended PET acquisition in PET/MRI rectal cancer staging improve results?

Jason J. Bailey, MD¹, Eric J. Jordan, MD¹, Colin Burke, MD¹, Michael A. Ohliger, MD PhD¹, Z. Jane Wang, MD¹, Katherine Van Loon, MD², Madhulika G. Varma, MD³, Thomas A. Hope, MD^{1,4,5}

¹Department of Radiology and Biomedical Imaging, University of California, San Francisco, San Francisco, CA

²Department of Medical Oncology, University of California, San Francisco, CA

³Department of Surgery, University of California, San Francisco, San Francisco, CA

⁴Department of Radiology, San Francisco VA Medical Center, San Francisco, San Francisco, CA

⁵Henry Diller Family Comprehensive Cancer Center, University of California, San Francisco, San Francisco, CA

Abstract

Purpose: To determine if extended PET acquisition times in the pelvis during PET/MRI increase detection rates of potentially metastatic lymph nodes for rectal cancer.

Methods: Study was approved by the local institutional review board. 22 subjects with biopsy-proven rectal cancer imaged via simultaneous 3.0 T time-of-flight PET/MRI, with 7 subjects undergoing two separate PET/MRI examinations, for a total of 29 studies. Each examination included both a whole body PET/MRI and a dedicated pelvis PET/MRI with both 3 and 15 minute PET acquisitions of the pelvis. Three radiologists interpreted each examination with PET only, MRI only, then combined PET and MRI examination, using all available images. Additionally, the 3 minute and 15 minute PET acquisitions of the pelvis were reviewed separately by a single radiologist.

Results: A total of 94 lymph nodes were identified as abnormal on PET imaging, all with MRI anatomic correlates. Of these, 37 (37/94, 39.4%) were seen only on the dedicated 15 minute acquisition. Fifty-seven (57/94) nodes measured 5 mm or less, including 29 (29/94, 30.9%) seen only on the 15 minute acquisition. Thirty-one (31/94) nodes measured 5.1–10 mm, including 8 (8/94, 8.5%) seen only on the 15 minute acquisition. Of the 17 subjects imaged for initial staging, 11 (11/18, 64.7%) were upstaged as a result of the increased PET acquisition time, 10 from N1 to N2, and 1 from N0 to N1.

Conclusion: Longer PET acquisition times during PET/MRI for rectal cancer increases the number of FDG avid lymph nodes detected without increasing scan time.

Keywords

Rectal cancer; PET/MRI; Acquisition time

Introduction

Accurate T-staging of rectal cancer has been significantly improved in recent years through the use of rectal magnetic resonance imaging (MRI), which provides high resolution imaging of the primary tumor and its relationship with the muscularis propria, mesorectal fascia, and local organs [1,2,3,4,5]. Despite the success of MRI in T-staging, nodal disease detection and accuracy remain limited, with high lymph node size cutoffs (> 1 cm) providing high specificity but poor sensitivity and low size cutoffs (> 5 mm) inevitably trading improved sensitivity for lower specificity [6,7,8,9,10,11]. Although adding morphologic features to a 5 mm size cutoff improves sensitivity and specificity [6,7,8,11,12,13], a more sensitive, specific, and reproducible method of identifying nodal metastases is needed.

The addition of [¹⁸F]-Fluorodeoxyglucose (FDG) positron emission tomography with computed tomography (PET/CT) has been shown to improve specificity for nodal disease detection in rectal cancer compared to high resolution MRI, and the combination of MRI with PET/CT has been shown to improve accuracy of malignant lymph node detection compared to either of those modalities alone [14]. The addition of FDG PET/CT has also been shown to frequently alter therapeutic management during initial staging [11,15,16,17,18,19]. Multiple studies suggest that FDG PET/CT provides additional staging information in rectal cancer, including improved sensitivity for lymph node and distant metastatic disease detection [19,20,21,22,23,24].

Simultaneous FDG PET/MRI combines the benefits of rectal MRI with metabolic information from PET in a single scan that can be superimposed during image interpretation. Early studies evaluating the ability of FDG PET/MRI to accurately stage rectal cancer suggest FDG PET/MRI may be more accurate than CT, MRI, and FDG PET/CT [25,26]. For detection of abnormal lymph nodes less than 1 cm, FDG PET/MRI may be particularly helpful, given the low sensitivity of MRI alone for these lymph nodes [5].

To improve the accuracy of FDG PET/MRI in the detection of hypermetabolic lymph nodes, imaging protocols should be optimized. Lengthening the PET acquisition time to increase detection of potentially metastatic lymph nodes has been shown to improve detection rates for other cancers with PET/MRI [27]. This study was designed to determine if extending PET acquisition time in the pelvis during dedicated pelvic MRI increases the detection rate of potentially metastatic lymph nodes for rectal cancer without increasing scan time.

Materials and Methods

Institutional review board approval with waived informed consent was obtained for this retrospective investigation. At the authors' home institution, the PET/MRI protocol for rectal cancer includes a whole body MRI with dedicated pelvic sequences, as well as both a 15 minute PET acquisition of the pelvis and a whole body PET acquisition composed of 3

minutes of PET imaging performed at each of 6 separate stations, one of them in the pelvis. The authors undertook a retrospective review of subjects scanned with this protocol for rectal cancer to evaluate if the 15 minute pelvic PET acquisition detected more potentially metastatic lymph nodes compared to the 3 minute pelvic PET acquisition.

A retrospective single institution search of the electronic medical record for PET/MRI studies performed in the setting of biopsy-proven rectal adenocarcinoma from January 1, 2015 to December 31, 2016 revealed a total of 29 PET/MRIs performed for 22 subjects (Table 1). Of 22 subjects, 17 were imaged for initial staging of rectal cancer, 5 for suspected recurrence, and 7 underwent a second PET/MRI examination for the purposes of restaging after chemotherapy and radiation therapy treatments. Subject characteristics are summarized in Table 1.

Imaging protocol

Patients were injected with 300.81 ± 59.2 MBq (8.13 ± 1.6 mCi) of FDG. Images were acquired on a simultaneous 3.0T time-of-flight PET/MRI (Signa, GE Healthcare), and imaging was performed 72.8 ± 22.3 min after injection. Two separate PET acquisitions were obtained during a single MRI acquisition: the first PET acquisition included a single bed position covering only the pelvis for 15 minutes. The second PET acquisition included a whole-body scan from the mid-thighs to the vertex, obtained for 3 minutes at each of six bed positions (18 minutes total). In the pelvis, all other parameters of the PET acquisitions besides time of acquisition were identical, including pixel size, voxel size, field of view, and area covered.

A whole body MRI as well as dedicated pelvic MRI sequences were obtained. The following MRI sequences were obtained of the pelvis:

1. Small field of view T2 (axial/coronal/sagittal): fast spin echo, flip angle = 125 degrees, slice thickness = 4.5 mm, number of slices per acquisition = 27, $T_E/T_R = 129/7567$ ms, NEX = 1.5, field of view (FOV) = 220×220 mm, acquisition matrix 448×256
2. Diffusion-weighted images (DWI): axial echo planar DWI, b values = 50 and 500 s/mm^2 , slice thickness = 6 mm, $TE/TR = 54/14117$ ms, matrix = 128×100
3. Dynamic contrast-enhanced (DCE) imaging with Differential Subsampling with Cartesian Ordering (DSCO) [28]: slice thickness = 2 mm, flip angle = 15 degrees, matrix = 512×512 , $TE_1/TE_2/TR = 2.0/4.1/5.6$ ms, NEX = 0.7, parallel imaging acceleration factors of 2 (phase direction) \times 2.5 (slice direction). Following a single injection (0.1 mmol/kg) of gadobutrol (Bayer Healthcare, Berlin, Germany), 17 phases were acquired every 11 s.
4. Post-contrast T1-weighted images (LAVA-FLEX): axial 3D spoiled gradient echo sequence using two-point Dixon LAVA flex, slice thickness = 3 mm, flip angle = 12 degrees, matrix size = 316×256 , $TE_1/TE_2/TR = 2.0/4.1/5.6$ ms, NEX = 0.7.

A whole-body MRI was also obtained at six bed positions while completed the whole-body PET scan, with three minutes per bed position of PET acquisition, as previously described which included a post-gadolinium LAVA-FLEX, and coronal and axial single shot fast spin echo sequences [27]. In the pelvis, attenuation correction was performed using a two point Dixon fat water separation algorithm, as supplied on the scanner [29].

Imaging interpretation

Three subspecialty-trained abdominal radiologists interpreted the PET/MRI examinations retrospectively, blinded to the previously reported results (JW, MO, TH). They were instructed to interpret each examination separately with PET images only, MR images only, then combined PET and MRI images, at separate sessions, separated by a minimum of one week. Lymph nodes were considered positive on PET if the reviewing radiologist considered them to demonstrate FDG uptake greater than background. Lymph nodes were considered positive on MRI if they demonstrated size greater than 5 mm in short axis dimension or abnormal morphology, e.g. spiculated borders or heterogeneous internal appearance [6]. The tumor stage (T-stage), number of abnormal lymph nodes, and nodal stage (N-stage) were recorded for each modality- PET alone, MR alone, and PET/MRI combined- using the American Joint Committee on Cancer (AJCC) TNM system [30].

Using the nodes detected by the three readers, the 3 minute and 15 minute PET acquisitions of the pelvis were separately reviewed by a fourth reader (CB), utilizing the corresponding high resolution T2-weighted MR sequence for anatomic localization. Visualized lymph nodes on MRI were again considered positive on PET if the reviewing radiologist considered them to demonstrate FDG uptake greater than background.

Statistical Analysis

Interreader variability calculations between the 3 reviewers were performed using Fleiss Kappa scores and interpreted using the Landis and Koch benchmark scale [31]. Statistical significance for interreader variability was calculated using Chi-Square test. Statistical analyses and calculations were performed by R (Vienna, Austria 2017) [32].

Results

Rates of lymph node identification on the 3 minute and 15 minute PET acquisitions are summarized in Table 2. Of the 29 studies, a total of 94 lymph nodes were identified as hypermetabolic on FDG-PET with a corresponding lymph node seen on MRI. Of these 94 lymph nodes, all 94 were seen on the 15 minute PET acquisition and 57 (55/94, 60.6%) were seen on the 3 minute PET acquisition, with 37 (37/94, 39.4%) lymph nodes seen only on the 15 minute PET acquisition (Figure 1).

When stratified by size, 57/94 (60.6%) abnormal lymph nodes were 5 mm or less, with 29/57 (50.8%) of these detected only on the 15 minute PET acquisition. 31/94 (32.9%) lymph nodes detected by PET were 5–10 mm, with 8/31 (25.8%) of these visible only on the 15 minute acquisition. Six lymph nodes greater than 10 mm were identified as hypermetabolic, with all 6 visible on both 3 minute and 15 minute PET acquisitions. 42%

(37/88) of lymph nodes identified as abnormal on the 15 minute PET acquisition would not have been identified on either the 3 minute PET acquisition or the pelvic MRI.

Rates of upstaging disease between 3 minute and 15 minute PET acquisitions are summarized in Table 3. Of the 17 subjects imaged for initial staging, 11 (11/17, 64.7) were upstaged, 10 (10/17, 58.9%) from N1 to N2, and 1 (1/17, 5.9%) from N0 to N1. Of the 29 total studies performed, 17 were upstaged (17/29, 58.6%), 15 (15/29, 51.7%) from N1 to N2, and 2 (2/29, 6.9%) from N0 to N1.

Interreader variability calculations are summarized in Table 4. T-staging using PET/MRI and N-staging using PET alone demonstrated substantial agreement, with kappa scores of 0.649 and 0.619, respectively. N-staging with PET/MRI and T-staging with MRI alone demonstrated moderate agreement, with kappa scores of 0.487 and 0.532, respectively. T-staging with PET alone and N-staging with MRI alone demonstrated fair agreement, with kappa values of 0.296 and 0.386, respectively.

Discussion

We demonstrated that performing a 15 minute extended PET acquisition in the pelvis detected more FDG avid lymph nodes, detecting 40% more lymph nodes than a standard 3 minute PET acquisition. Using a 15 minute PET acquisition instead of a 3 minute acquisition resulted in nodal upstaging in over half of the patients. Our study also suggests that interreader variability is lower between PET/MRI readers compared to MRI alone.

Our results are concordant with previous work suggesting that extended PET acquisition times can increase detection of small lesions, for example in prostate cancer [27]. The explanation for increased detection with longer PET acquisitions is likely the improved emission counts for each voxel, which improves signal-to-noise ratio and makes abnormal lymph nodes easier for the radiologist to identify. The abnormal lymph nodes identified only on the 15 minute PET acquisition were likely present on the 3 minute acquisition but indistinguishable (or at least very difficult to distinguish from) noise on the PET images. In PET/CT, where typical z-axis field of views are 15 cm, most groups do not image for longer than 3 minutes at each bed position. Both clinically available PET/MRIs have a 25 cm z-axis field of view, which allows for nearly double the acquisition segment at each bed position without altering the overall scan time. Additionally, in PET/MRI, the MRI pulse sequences are the rate limiting step, meaning an increase in PET acquisition time does not actually increase overall PET/MRI scan time. In our protocol, we chose to image for 15 minutes at the rectal bed position due to the numerous bed specific MRI pulse sequences that are required for rectal cancer.

This study has multiple limitations. Firstly, our study has a small sample size, limited by PET/MRI being an emerging and novel technique in rectal cancer. Additionally, our study lacks correlation with pathologic staging. Given the small percentage of patients that had undergone surgery at the time of the study completion, comparison with pathology results was not yet feasible. It is certainly possible that increasing the PET acquisition time detects not just more abnormal lymph nodes but also more normal lymph nodes. For future

investigation on this topic, a larger study population with post-surgical pathology as a gold standard should be considered.

Conclusion

Longer pelvis PET acquisitions during a simultaneous PET/MRI performed for rectal cancer detects an increased number of FDG avid pelvic lymph nodes and increases detection and upstaging of metastatic disease.

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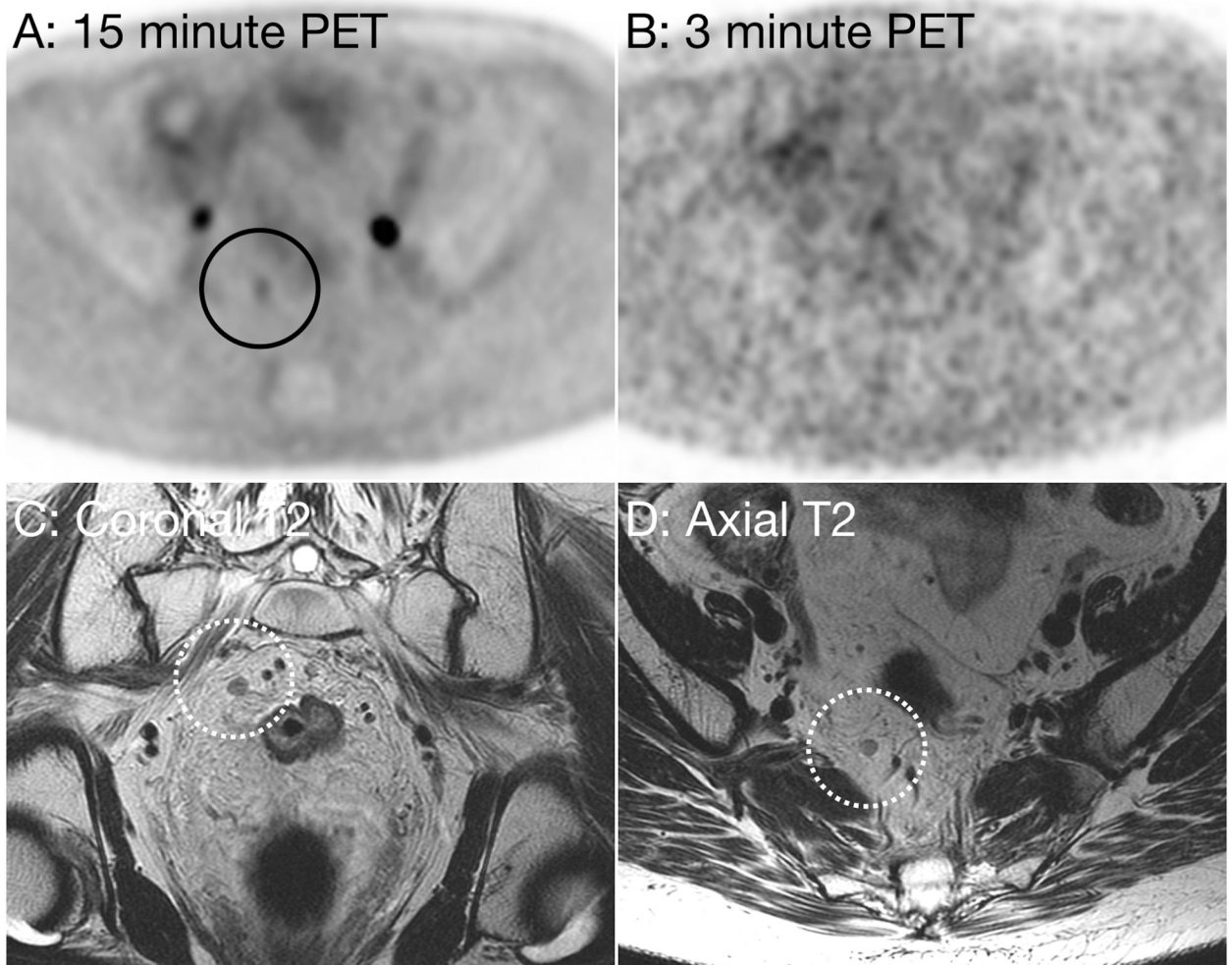


Figure 1:
53 year-old woman with metastatic rectal carcinoma. Axial PET image using a 15 minute acquisition time (Figure A, black circle) demonstrate a focus of abnormal hypermetabolism, suspicious for a metastatic lymph node. Axial PET image performed using a 3 minute acquisition time (B) does not demonstrate abnormal FDG uptake. Oblique coronal (D, dotted white circle) and oblique axial (C, dotted white circle) small field of view T2 weighted images demonstrate a right mesorectal lymph node measuring 4 mm in short axis without suspicious morphologic features.

Table 1:

Subject characteristics (n = 29)

Average Age (years):	56.6±10.9
Gender:	
Male:	13 (13/29, 44.8%)
Female:	16 (16/29, 55.2%)
FDG Dose (mCi):	8.1±1.6
Time from Injection to Imaging (min):	72.8±22.3

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Table 2:

Hypermetabolic lymph nodes identified on 3 minute and 15 minute PET/MRI acquisitions (n = 94)

	3 minute acquisition	15 minute acquisition	15 minute acquisition only
Total	57 (57/94, 60.6%)	94 (100%)	37 (37/94, 39.4%)
5 mm or smaller (57/94, 60.6%)	28 (28/57, 49.1%)	57 (100%)	29 (29/57, 60.6%)
5.1–10 mm (31/94, 34.1%)	23 (23/31, 74.1%)	31 (100%)	8 (8/31, 25.8%)
> 10 mm (6/94, 6.4%)	6 (100%)	6 (100%)	0

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Table 3:

Distribution of nodal disease staging based on 3 minute and 15 minute PET/MRI acquisitions during initial staging exams (n = 17) and for all studies (n = 29)

	Initial staging (n=17)	Initial staging (n=17)	All studies (n=29)	All studies (n=29)
	3 minute acquisition	15 minute acquisition	3 minute acquisition	15 minute acquisition
N0	2 (2/17, 11.8%)	1 (1/17, 5.9%)	3 (3/29, 10.3%)	1 (1/29, 3.4%)
N1	15 (15/17, 88.2%)	6 (6/17, 35.3%)	24 (24/29, 82.8%)	11 (11/29, 37.9%)
N2	0	10 (10/17, 58.8%)	2 (2/29, 6.9%)	17 (17/29, 58.6%)

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Table 4:

Interreader variability assessment of PET/MRI performed for rectal cancer in Kappa Values (Agreement grades using Landis and Koch benchmark scale).

	T Staging	N Staging
PET/MRI	0.65	0.49
PET Alone	0.30	0.62
MRI Alone	0.53	0.39

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