Evaluation of the tumor registration error in biopsy procedures performed under real-time PET/CT guidance

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Purpose: The purpose of this study is to quantify tumor displacement during real-time PET/CT guided biopsy and to investigate correlations between tumor displacement and false-negative results.

Methods: 19 patients who underwent real-time ¹⁸F-FDG PET-guided biopsy and were found positive for malignancy were included in this study under IRB approval. PET/CT images were acquired for all patients within minutes prior to biopsy to visualize the FDG-avid region and plan the needle insertion. The biopsy needle was inserted and a post-insertion CT scan was acquired. The two CT scans acquired before and after needle insertion were registered using a deformable image registration (DIR) algorithm. The DIR deformation vector field (DVF) was used to calculate the mean displacement between the pre-insertion and post-insertion CT scans for a region around the tip of the biopsy needle. For 12 patients one biopsy core from each was tracked during histopathological testing to investigate correlations of the mean displacement between the two CT scans and false-negative or true-positive biopsy results. For 11 patients, two PET scans were acquired; one at the beginning of the procedure, pre-needle insertion, and an additional one with the needle in place. The pre-insertion PET scan was corrected for intraprocedural motion by applying the DVF. The corrected PET was compared with the post-needle insertion PET to validate the correction method.

Results: The mean displacement of tissue around the needle between the pre-biopsy CT and the postneedle insertion CT was 5.1 mm (min = 1.1 mm, max = 10.9 mm and SD = 3.0 mm). For mean displacements larger than 7.2 mm, the biopsy cores gave false-negative results. Correcting pre-biopsy PET using the DVF improved the PET/CT registration in 8 of 11 cases.

Conclusions: The DVF obtained from DIR of the CT scans can be used for evaluation and correction of the error in needle placement with respect to the FDG-avid area. Misregistration between the pre-biopsy PET and the CT acquired with the needle in place was shown to correlate with false negative biopsy results. © 2017 American Association of Physicists in Medicine [https://doi.org/10.1002/mp.12334]

Key words: biopsy, image registration, image-guidance, oncology, PET/CT

1. INTRODUCTION

Obtaining an adequate tissue biopsy for microscopic examination is essential for rendering an accurate pathologic diagnosis in cancer patients. However, the success of biopsy procedures is often limited by sampling errors due to imprecise placement of the biopsy needle. Biopsy image guidance using anatomic imaging, e.g., ultrasound or CT, can reduce these errors. In addition, metabolic images like PET can be used to guide interventions for lesions that are not easily seen on anatomic images.¹ Fusion of CT with PET images allows

physicians to identify and biopsy a metabolically active lesion before morphologic changes can be observed.²

In the case of PET/CT guided biopsies the success depends on accurate positioning of the needle relative to the FDG-avid lesion. Until recently, PET/CT-guided biopsies were performed using a preprocedural PET scan acquired several days prior to the biopsy. Such is the investigation by Guralnik et al., who showed that the distance between the location of the needle tip and the lesion highest SUV was significantly higher for false-negative results ($15.4 \text{ mm} \pm 14 \text{ mm}$) than for true-positive ($5.9 \pm 13.4 \text{ mm}$).³ To achieve high precision in positioning of

the needle, an accurate PET/CT registration is needed. However, changes in size, shape, or metabolic characteristics of the lesion can occur during the time interval between the preprocedural PET and the intraprocedural CT, which can lead to image misregistration.⁴⁻⁷ Also, patient position may vary between two acquisitions making registration challenging and suboptimal.³ More recently and with the availability of PET/CT in the interventional suite, biopsies can be performed with real-time intraprocedural PET/CT guidance, which has been shown to reduce PET/CT misregistration.⁸⁻¹¹ While real-time PET/CT guidance allows overcoming some of the above limitations, intraprocedural motion and organ displacement due to needle push can still lead to PET/CT misregistration and false-negative results.

Previous studies sought to evaluate the benefits and accuracy of PET/CT-guided biopsy but the intraprocedural patient and organ motion due to needle push was not measured. Guralnik et al.³ selected only patients for whom good registration was obtained between the PET/CT scans acquired a few days before and the CT performed during the biopsy procedure. Shyn et al. studied the effect of breathing on PET/CT registration for tumors near the diaphragm during real-time PET/CT guided biopsy but all the scans were acquired before needle insertion.¹² In another study investigating the benefits of PET/CT over CT only guided biopsy, the quality of the PET/CT registration was not mentioned.⁷

In this study, a method to evaluate the magnitude of intraprocedural motion leading to PET/CT misregistration during real-time PET/CT-guided biopsies is proposed, as well as a method for motion correction of the PET acquired at the beginning of the procedure. If motion occurs and the registration is not satisfying, a second PET scan can be performed. However, acquiring an additional PET image increases the procedure length, which could potentially lead to a higher risk of complication. Longer procedure times also increase patient's discomfort and in general could result in patient motion. Lastly, correlations between image misregistration and false-negative result were investigated in order to search for a threshold above which the registration is not reliable and a second PET should be acquired to improve the biopsy accuracy.

2. MATERIALS AND METHODS

2.A. Patients

The method to quantify patient motion and organ shifts due to needle insertion was developed using data from nineteen patients undergoing a real-time PET/CT-guided biopsy under an institutional review board-approved study, which complied with the Health Insurance Portability and Accountability Act. The lesions were not seen on the CT images so the targeting was based on the PET images only. Of these nineteen patients, fifteen were biopsies in the liver, two were in the lung, one was in the spleen, and one was in soft tissue near the left scapula. Biopsy cores were obtained with 18-gauge or 20-gauge needles. The diagnosis was made based on all the extracted cores, with an average of about three

cores per patient. All patients included in this study were found positive for malignancy.

2.B. PET/CT guided biopsy procedure

The clinical workflow of patients undergoing real-time PET/CT-guided biopsy is shown in Fig. 1. A whole-body CT and PET scan (noted CT_{pre} and PET_{pre}) are acquired at the beginning of the biopsy procedure. CT_{pre} and PET_{pre} are fused to allow for the interventional radiologist to localize the FDG-avid lesion relatively to anatomical structures. The biopsy needle is then inserted with the help of fluoroscopy. An additional CT (referred to as CT_{needle}) is acquired with the needle in place and fused with PET_{pre} . The position of the needle relatively to the FDG-avid lesion can then be visualized.

A biopsy sample is extracted when the fused PET/CT image shows the needle to be inside the FDG-avid lesion. If that condition is not met, the needle is repositioned and another CT is acquired until adequate positioning is obtained. Immediately after extraction of a biopsy specimen, a rapid on-site evaluation (ROSE) of the specimen is performed by a cytologist. This allows evaluating if the specimen is adequate and if sufficient amount of tissue for diagnosis is obtained. If the first biopsy core is found inadequate by the cytologist, the biopsy needle is repositioned and another core is extracted. Therefore, the number of biopsy specimens extracted from a patient depends on the needle placement i.e., if the needle is placed in the lesion at the first attempt, and on how confident the cytologist is that an adequate core is obtained.

2.C. PET/CT acquisition

PET/CT guided biopsy procedures were performed in an interventional radiology suite on a PET/CT scanner (Discovery 690, GE Healthcare, Waukesha, WI, USA). Patients were injected with 160–225 MBq of ^{18}F -FDG and patients were under sedation or anesthesia. An initial CT and a free-breathing PET were acquired after an uptake time ranging from 60 to 150 min. The initial PET/CT was used to plan the intervention. In order to reduce the dose to the patient, additional CT scans acquired after needle insertion for a limited region of interest (ranging from 25 to 65 mm in length) and at a higher pitch factor than that for the initial CT. The initial CT was reconstructed to $1.37 \times 1.37 \times 3.27 \text{ mm}^3$ voxels and additional CTs were reconstructed to $0.877 \times 0.877 \times 5.00 \text{ mm}^3$ voxels. CT_{pre} was used for PET_{pre} attenuation correction. The initial PET was reconstructed to $5.47 \times 5.47 \times 3.27 \text{ mm}^3$ voxels.

For 11 patients, an additional PET (noted PET_{needle}) was acquired subsequently to CT_{needle} . The initial CT, CT_{pre} , was used for attenuation correction of PET_{needle} since CT_{needle} can be affected by streak artifact due to the presence of the biopsy needle and due to the lower quality of CT_{needle} .¹³ The location of the needle relative to the FDG-avid lesion was visualized on the fused CT_{needle}/PET_{needle} scans [Fig. 1(b)].

The PET/CT images were inherently co-registered, using the same local coordinates. For this study, the PET scans were

FIG. 1. Clinical Workflow of a real-time PET/CT guided biopsy without (a) and with a second PET scan (b). Images from Patient 12 are shown for illustration. In part (a) is shown the workflow when only one PET scan is performed right before needle insertion and in part (b) is explained the workflow when an additional PET scan is acquired after needle insertion. In both cases an initial PET/CT (PET_{pre}/CT_{pre}) was acquired and fused to plan the needle insertion. Once the needle was inserted; in case (a) an additional CT was acquired (CT_{needle}) and fused with the initial PET_{pre} or in case (b) a CT plus and additional PET were acquired and fused (CT_{needle}/PET_{needle}). [Color figure can be viewed at wileyonlinelibrary.com]

up-sampled from 128×128 to 512×512 using a linear interpolation to better match the CT images that more accurately identify the position of the biopsy needle.

2.D. Deformable image registration

CT_{pre} was registered to CT_{needle} using a fast free-form deformable registration algorithm¹⁴ implemented in an in-house research 3-dimensional (3D) treatment planning system (Metropolis).¹⁵ The displacement vector field (DVF) was obtained in 3D and the mean displacement in a volume of interest (130 cm^3 in average) around the needle was calculated (Fig 2). The volume of interest was manually selected, in order to include the needle tip and the FDG-avid lesion. The size of the volume of interest depends therefore on the inclination of the needle and the size of the lesion. The mean 3D displacement is an estimate of the magnitude of patient and organ motion between CT_{pre} and CT_{needle} in a region around the biopsy needle.

2.E. Misregistration and biopsy adequacy

For the purpose of the study, one of the cores extracted was marked with a tissue marking dye for 12 patients of the 19 patients. This allows tracking this particular core during histopathology examination. The concurrent CT_{needle} scan

showing the positioning of the needle right before extraction of the core was recorded for later analysis. The 12 inked-cores were embedded in paraffin, sectioned into $4 \mu\text{m}$ -thick slides and stained with hematoxylin and eosin (H&E) for histopathology evaluation. Correlations of the mean displacement between CT_{pre} and CT_{needle} with the presence or absence of malignant cells in the inked biopsy core were investigated. It is important to note that all 12 patients were found positive for malignancy from evaluation based on multiple cores but the ink-marked cores only were used for correlation between image misregistration and biopsy adequacy.

2.F. Motion correction of PET images

To correct the initial PET scan for intraprocedural patient and organ motion, the DVF calculated from CT_{pre} and CT_{needle} registration was applied to PET_{pre} . The obtained PET is referred to as $PET_{corrected}$. This motion correction method was tested on the eleven patients for whom two PET scans (before and after needle insertion) were acquired. $PET_{corrected}$ was compared to the reference image, PET_{needle} . To quantify this correction, the three PET image datasets (PET_{pre} , PET_{needle} , $PET_{corrected}$) were segmented using the Fuzzy Locally Adaptive Bayesian (FLAB) algorithm. The FLAB algorithm is based on a fuzzy C-means clustering algorithm and Bayesian probability. It has been shown to be

FIG. 2. Displacement vector field displayed on top of a transverse CT_{needle} image. The black rectangle defines the ROI around the needle, inside which the mean displacement was calculated. For reference the needle notch (thin part near needle end) is 2 cm long. [Color figure can be viewed at wileyonlinelibrary.com]

independent of the anatomical site and to be accurate, robust, and reproducible.^{16–19} The segmentation contours obtained for patient 12 for the three PET scans and the distance d between the middle of the biopsy needle notch and the center of mass of the segmentation contour for CT_{needle}/PET_{needle} are shown in Fig. 3. The distance d of each segmented contour was measured on the fused CT_{needle}/PET_{pre} , CT_{needle}/PET_{needle} , $CT_{needle}/PET_{corrected}$ images [Fig. 4(b)].

3. RESULTS

3.A. Image displacement

Image registration using the fast-free form deformable registration took less than 3 min. The algorithm seemed to perform well in the vicinity of the needle and not to be affected by the difference of resolution and noise between CT_{pre} and CT_{needle} . For the 19 patients included in this study, the mean displacement over a region of interest defined around the needle as obtained from the CT deformation vector field was 5.1 mm (with min = 1.1 mm, max = 10.9 mm and standard deviation = 3.0 mm).

3.B. Biopsy adequacy

The presence or absence of malignant cells in the inked biopsy specimen as a function of the mean displacement

between CT_{pre} and CT_{needle} is shown in Table I. It shows that above a threshold of 7.2 mm the core obtained did not contain any malignant cells whereas the PET_{pre}/CT_{needle} image showed the needle to be in the FDG-avid lesion. For a mean displacement of 6.2 mm and under, the biopsy yielded a true-positive result.

3.C. Motion correction

The position of the centers of gravity of the segmented PET regions and their distances from the needle notch were used to evaluate the registration errors of the PET images. For the eleven patients with a second PET, the mean areas of the segmented regions in the slice of interest containing the needle for PET_{pre} , $PET_{corrected}$, and PET_{needle} were, respectively, 1.6 cm² (min: 0.50 cm², max 2.6 cm², std 0.61 cm²), 1.7 cm² (min 0.40 cm², max 2.3 cm², std 0.52 cm²), and 1.4 cm² (min 0.25 cm², max 2.4 cm², std 0.76 cm²). In Fig. 4 are plotted the differences in the distances between the needle notch and the center of gravity of the PET avid area in the reference image, CT_{needle}/PET_{needle} , and the respective distances in CT_{needle}/PET_{pre} versus that difference for $CT_{needle}/PET_{corrected}$. If the deformation correction applied to PET_{pre} is accurate, the difference in the distance between CT_{needle}/PET_{needle} and $CT_{needle}/PET_{corrected}$ will be smaller than the difference in the distance between CT_{needle}/PET_{needle} and CT_{needle}/PET_{pre} . Hence, every point above the line $x=y$ shows that applying the deformation correction to PET_{pre} image makes it closer to the reference image. Figure 4 shows that in 8 of 11 cases, applying the deformation correction to PET_{pre} reduces the registration error. For two cases, no improvement was observed and for one case the registration error is 1 mm higher after correction.

4. DISCUSSION

The goal of this study was to determine the registration error between the PET scan acquired at the beginning of the procedure and the CT acquired with the needle in place, to develop a correction for it and to evaluate how misregistration affects biopsy outcome. Our findings indicate that PET/CT misregistration leads to false-negative biopsy results above a certain registration error threshold. The mean needle displacement resulting from such misregistration could be calculated automatically after CT_{needle} acquisition and made available to the interventional radiologist. The interventional radiologist can then decide whether the registration is accurate and reliable or whether a second PET should be acquired. The displacement threshold leading to false negative results was estimated to be 7.2 mm from a small patient cohort and needs to be refined using a larger number of cases. This threshold is in agreement with previously published numbers. In a study of 267 patients undergoing a lung biopsy guided by a preprocedural FDG PET/CT and for whom good registration with the procedural CT was obtained, the distance between the needle tip and the area with the highest metabolic activity was 15.4 ± 14 mm for patients with false

FIG. 3. The Fuzzy locally adaptive Bayesian (FLAB) segmentation contours obtained for PET_{pre} , PET_{needle} , and $PET_{corrected}$ are displayed in green, red, and blue, respectively, on top of the fused (a) CT_{needle}/PET_{pre} ; (b) CT_{needle}/PET_{needle} ; (c) $CT_{needle}/PET_{corrected}$; (d) The three PET segmentation contours are displayed on top of the CT_{needle} image (zoomed). The distance d between the middle of the notch of the needle (seen as voxels in white color on the CT_{needle} image) and the center of mass of the PET_{needle} segmentation contour is shown for illustration. These scans were obtained from patient 12. [Color figure can be viewed at wileyonlinelibrary.com]

FIG. 4. (a) The distance between the biopsy needle seen in the CT_{needle} and the center of mass of the segmentation contour of PET_{needle} is compared to the same distance as obtained for PET_{pre} , and $PET_{corrected}$. The plot shows that the corrected PET image is closer to the PET image with the needle for most cases. (b) Illustration of how the distance d between the needle notch and the PET segmentation contour center of mass is measured. The segmentation contours in the different images are illustrated by different color circles. [Color figure can be viewed at wileyonlinelibrary.com]

negative results compared to 5.9 ± 13.4 mm for patients with true positive results.³

The mean displacements between CT_{pre} and CT_{needle} over a ROI around the needle can be attributed to patient motion

between the two CT scans, or organ displacement due to pressure from the needle insertion. Areas of the body that are most subject to respiratory and cardiac motion are mainly the organs of the thorax and abdomen,^{20–22} which correspond

TABLE I. Mean displacement between CT_{pre} and CT_{needle} over a ROI around the biopsy needle for the 12 patients for which histopathology correlation was investigated. The presence or absence of tumor cells in the biopsy sample extracted immediately after CT_{needle} acquisition is shown in column 3.

Patient #	Mean displacement over an ROI around the needle between CT_{pre} and CT_{needle} (mm)	Presence (1) or absence (0) of tumor cells
1	1.1	1
2	2.5	1
3	2.9	1
4	3.0	1
5	3.5	1
6	4.0	1
7	4.9	1
8	6.2	1
9	7.5	0
10	7.9	0
11	9.7	0
12	10.7	0

to the organs biopsied for the patients included in this study. A study performed by Shyn et al. report that during PET/CT-guided biopsy or ablation of lesions located near the diaphragm, mean misregistration in the transverse plane was 2.6 mm (range, 0–8 mm) with monitoring respiratory motion and 4.0 mm (range, 0–12 mm) without monitoring.¹² PET and CT have different accumulation times (less than a minute for the CT and several minutes for the PET), which may introduce motion blurring and distortion of moving lesions imaged by PET. If the lesion is moving over a breathing cycle, the PET image will be the integration over time of the activity detected at each location, increasing the apparent size of the lesion.²³

The challenges faced when trying to register CT_{pre} and CT_{needle} come from the presence of the biopsy needle in CT_{needle} and not in CT_{pre} and the difference in resolution and noise level between the two images. The deformable image registration used in this study showed good performance with this particular type of data. The objective function for deformable registration includes a regularization term for the displacement field that penalizes the deviation of displacement vectors of neighboring voxels. Using a multiresolution paradigm also provides for a smooth displacement field. Moving the voxels corresponding to the needle in the CT in which the needle is not present does not significantly affect the intensity in the objective function, but affects the smoothness of the displacement field. Thus, the needle voxels tend to move with the movement of the surrounding soft tissue. In addition, due to the regularization term and the use of multiresolution approach the algorithm is not sensitive to noise.

The method proposed for motion correction can be applied in real time in order to obtain a more accurate PET/CT registration without the burden of an additional PET scan acquisition. When using this technique, improvements were observed in 8 out of 11 cases. The lack of improvement in three cases may be due to: (a) motion between the acquisition

of CT_{needle} and PET_{needle} ; (b) the difference in the uptake period between PET_{pre} and PET_{needle} , which can be about an hour and could result in different FDG uptake in the lesion; (c) performance limitations of the fast free-form algorithm. Testing the method on a larger patient cohort is needed before using it clinically.

PET_{needle}/CT_{needle} was considered as the reference image but motion can occur between the PET_{needle} and the CT_{needle} acquisition, since they are acquired sequentially.²⁴ The chances for motion between PET_{needle} and CT_{needle} are, however, less compared to PET_{pre}/CT_{pre} since PET_{needle} and CT_{needle} are acquired for a shorter length of time. One way to verify position of the needle in PET_{needle} would be to visualize the biopsy needle in the PET image. A similar approach was investigated and reported by Prior et al. for a patient undergoing a PET/CT-guided radiofrequency ablation of liver metastases.²⁵ A 20-gauge cannula filled with ^{18}F -FDG was inserted into the wider coaxial cannula used to insert the radiofrequency electrode in the lesion. The radioactive cannula was visible on both the PET and the CT images. The location of the radiofrequency electrode probe in the PET image could therefore be determined accurately by extrapolation of the trajectory of the ^{18}F -filled cannula.

As stated in the method section, PET_{needle} was corrected for photon attenuation using CT_{pre} , since CT_{needle} was acquired with a lower dose and poorer quality and the presence of the needle in the CT_{needle} makes the latter suboptimal for attenuation-correction. This implies that when motion occurs between the two acquisitions, the attenuation correction will introduce quantitative errors in the PET_{needle} image.²⁶ One way of testing if using CT_{pre} introduces quantification error in PET_{needle} would be to apply the deformation vector field to CT_{pre} and to reconstruct PET_{needle} with the corrected CT_{pre} . However, we expect the attenuation correction error to be low for lesions located in organs which like the liver have homogeneous density and the attenuation is uniform.

Finally, we mention that while we have been using our standard PET reconstruction protocol (128×128 image matrix), a PET/CT biopsy PET reconstruction specific protocol using a finer reconstruction matrix (e.g., 256×256) would allow to more accurately identify the position of the biopsy needle in the PET image.

5. CONCLUSIONS

The deformation vector field obtained from registering the CT acquired at the beginning of the procedure to the CT with the needle in place, allows for evaluation of the error in needle placement with respect to the metabolic center of the lesion for real time PET/CT guided biopsy procedures. It may also be considered for a correction of the PET images and to evaluate if a second PET is needed, however, further validation with more patients is needed in order to recommend this approach. The magnitude of the deformation vector field was shown to correlate with inadequate biopsy samples.

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CONFLICTS OF INTEREST

The authors have no relevant conflicts of interest to disclose.

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REFERENCES

- Kobayashi K, Bhargava P, Raja S, et al. Image-guided biopsy: what the interventional radiologist needs to know about PET/CT. *Radiographics*. 2012;32:1483–1501.
- Aizhi Zhu DL, Shim Hyunsuk. Metabolic PET imaging in cancer detection and therapy response. *Semin Oncol*. 2011;38:55–69.
- Guralnik L, Rozenberg R, Frenkel A, Israel O, Keidar Z. Metabolic PET/CT-guided lung lesion biopsies: impact on diagnostic accuracy and rate of sampling error. *J Nucl Med*. 2015;56:518–522.
- Tatli S, Gerbaudo VH, Mamede M, Tuncali K, Shyn PB, Silverman SG. Abdominal masses sampled at PET/CT-guided percutaneous biopsy: initial experience with registration of prior PET/CT images. *Radiology*. 2010;256:305–311.
- Abi-Jaoudeh N, Mielekamp P, Noordhoek N, et al. Cone-beam computed tomography fusion and navigation for real-time positron emission tomography-guided biopsies and ablations: a feasibility study. *J Vasc Interv Radiol*. 2012;23:737–743.
- Venkatesan AM, Kadoury S, Abi-Jaoudeh N, et al. Real-time FDG PET guidance during biopsies and radiofrequency ablation using multimodality fusion with electromagnetic navigation. *Radiology*. 2011;260:848–856.
- Yokoyama K, Ikeda O, Kawanaka K, et al. Comparison of CT-guided percutaneous biopsy with and without registration of prior PET/CT images to diagnose mediastinal tumors. *Cardiovasc Interv Radiol*. 2014;37:1306–1311.
- Tatli S, Gerbaudo VH, Feeley CM, Shyn PB, Tuncali K, Silverman SG. PET/CT-guided percutaneous biopsy of abdominal masses: initial experience. *J Vasc Interv Radiol*. 2011;22:507–514.
- Aparici CM, Aslam R, Win AZ. Initial experience of utilizing real-time intra-procedural PET/CT biopsy. *J Clin Imaging Sci*. 2014;4:54.
- Cerci JJ, Neto CCP, Krauzer C, Sakamoto DG, Vitola JV. The impact of coaxial core biopsy guided by FDG PET/CT in oncological patients. *Eur J Nucl Med Mol Imaging*. 2013;40:98–103.
- Fanchon LM, Dogan S, Moreira AL, et al. Feasibility of in situ, high-resolution correlation of tracer uptake with histopathology by quantitative autoradiography of biopsy specimens obtained under 18F-FDG PET/CT guidance. *J Nucl Med*. 2015;56:538–544.
- Shyn PB, Tatli S, Sainani NI, et al. Minimizing image misregistration during PET/CT-guided percutaneous interventions with monitored breath-hold PET and CT acquisitions. *J Vasc Interv Radiol*. 2011;22:1287–1292.
- Stattaus J, Kuehl H, Ladd S, et al. CT-Guided biopsy of small liver lesions: visibility, artifacts, and corresponding diagnostic accuracy. *Cardiovasc Interv Radiol*. 2007;30:928–935.
- Lu W, Chen ML, Olivera GH, Ruchala KJ, Mackie TR. Fast free-form deformable registration via calculus of variations. *Phys Med Biol*. 2004;49:3067–3087.
- Jeong J, Chen Q, Febo R, et al. Adaptation, commissioning, and evaluation of a 3D treatment planning system for high-resolution small-animal irradiation. *Techn Cancer Res Treat*. 2015;6.
- Hatt M, le Rest CC, Turzo A, Roux C, Visvikis D. A fuzzy locally adaptive bayesian segmentation approach for volume determination in PET. *IEEE Trans Med Imaging*. 2009;28:881–893.
- Hatt M, leCheze- Rest C, vanBaardwijk A, Lambin P, Pradier O, Visvikis D. Impact of tumor size and tracer uptake heterogeneity in (18)F-FDG PET and CT non-small cell lung cancer tumor delineation. *J Nucl Med*. 2011;52:1690–1697.
- Hatt M, Cheze le Rest C, Descourt P, et al. Accurate automatic delineation of heterogeneous functional volumes in positron emission tomography for oncology applications. *Int J Radiat Oncol Biol Phys*. 2010;77:301–308.
- Hatt M, Cheze Le Rest C, Albarghach N, Pradier O, Visvikis D. PET functional volume delineation: a robustness and repeatability study. *Eur J Nucl Med Mol Imaging*. 2011;38:663–672.
- Langen KM, Jones DT. Organ motion and its management. *Int J Radiat Oncol Biol Phys*. 2001;50:265–278.
- Goerres GW, Burger C, Schwitter MR, Heidelberg TN, Seifert B, von Schulthess GK. PET/CT of the abdomen: optimizing the patient breathing pattern. *Eur Radiol*. 2003;13:734–739.
- Brandner ED, Wu A, Chen H, et al. Abdominal organ motion measured using 4D CT. *Int J Radiat Oncol Biol Phys*. 2006;65:554–560.
- Soret M, Bacharach SL, Buvat I. Partial-volume effect in PET tumor imaging. *J Nucl Med*. 2007;48:932–945.
- Beyer T, Antoch G, Muller S, et al. Acquisition protocol considerations for combined PET/CT imaging. *J Nucl Med*. 2004;45:25S–35S.
- Prior JO, Kosinski M, Delaloye AB, Denys A. Initial report of PET/CT-guided radiofrequency ablation of liver metastases. *J Vasc Interv Radiol*. 2007;18:801–803.
- Kinahan PE, Hasegawa BH, Beyer T. X-ray-based attenuation correction for positron emission tomography/computed tomography scanners. *Semin Nucl Med*. 2003;33:166–179.