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PET/CT-guided percutaneous liver mass biopsies and ablations: Targeting accuracy of a single 20 s breath-hold PET acquisition

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AIM: To determine whether a single 20 s breath-hold positron-emission tomography (PET) acquisition obtained during combined PET/computed tomography (CT)-guided percutaneous liver biopsy or ablation procedures has the potential to target 2-[^{18}F]-fluoro-2-deoxy-D-glucose (FDG)-avid liver masses as accurately as up to 180 s breath-hold PET acquisitions.

MATERIALS AND METHODS: This retrospective study included 10 adult patients with 13 liver masses who underwent FDG PET/CT-guided percutaneous biopsies ($n = 5$) or ablations ($n = 5$). PET was acquired as nine sequential 20 s, monitored, same-level breath-hold frames and CT was acquired in one monitored breath-hold. Twenty, 40, 60, and 180 s PET datasets were reconstructed. Two blinded readers marked tumour centres on randomized PET and CT datasets. Three-dimensional spatial localization differences between PET datasets and either 180 s PET or CT were analysed using multiple regression analyses. Statistical tests were two-sided and $p < 0.05$ was considered significant.

RESULTS: Targeting differences between 20 s PET and 180 s PET ranged from 0.7–20.3 mm (mean 5.3 ± 4.4 mm; median 4.3) and were not statistically different from 40 or 60 s PET ($p = 0.74$ and 0.91, respectively). Targeting differences between 20 s PET and CT ranged from 1.4–36 mm (mean 9.6 ± 7.1 mm; median 8.2 mm) and were not statistically different from 40, 60, or 180 s PET ($p = 0.84$, 0.77, and 0.35, respectively).

CONCLUSION: Single 20 s breath-hold PET acquisitions from PET/CT-guided percutaneous liver procedures have the potential to target FDG-avid liver masses with equivalent accuracy to 180 s summed, breath-hold PET acquisitions and may facilitate strategies that improve image registration and shorten procedure times.

Introduction

The use of combined positron-emission tomography/computed tomography (PET/CT) as a guidance method for interventional radiology procedures has been shown to enable targeting of tumours that are not well visualized at CT or other imaging methods.[1–3] The radiopharmaceutical 2-[^{18}F]-fluoro-2-deoxy-D-glucose (FDG) can be used to

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distinguish benign from malignant masses, viable from non-viable, or biologically aggressive from non-aggressive regions of malignant masses.[4] The potential to target masses or specific regions of masses using other radiopharmaceuticals that facilitate PET imaging of various molecular markers, for example, those associated with cell proliferation, apoptosis, hypoxia, and others, suggests a wide range of possibilities for interventional PET/CT-guided procedures in the future.[4]

The use of PET/CT guidance for interventional radiology procedures poses unique challenges. Diagnostic PET images are routinely acquired as 1–5 min acquisitions for each bed position.[5] These acquisitions are too long for single breath-holds and are obtained during continuous breathing. Consequently, PET images are subject to respiratory motion artefacts that include distortions of lesion size, shape, or spatial location, and reductions in FDG standardized uptake value (SUV) measurements.[6] Routine PET acquisitions during continuous breathing may prolong procedure times and the amount of time a patient is sedated or anaesthetized.

PET/CT is subject to image misregistration due to the sequential acquisition of PET and CT images.[7] PET/CT image misregistration is important as percutaneous biopsy needles or ablation devices are typically visible only on CT images, whereas the target may be visible only on PET images. As a result, PET/CT image misregistration may reduce the accuracy with which liver masses can be targeted.[8] Optimal image registration is also important when PET/CT is used to assess the ablation margin during ablation procedures, given that the tumour is persistently FDG-avid on PET and the ablation zone can be demonstrated at contrast-enhanced CT.[9]

Three-minute breath-hold PET images can be generated by summing multiple short PET frames, each obtained at the same breath-hold level.[8,10] This approach has been shown to minimize PET respiratory motion artefacts and PET/CT image misregistration.[8] Although these advantages of breath-hold PET/CT techniques in interventional radiology have been demonstrated, the disadvantages of requiring multiple breath-holds include difficulty in patient cooperation, variations in successive breath-holding levels, and longer procedure times. The purpose of this study was to determine whether a single 20 s breath-hold PET acquisition obtained during PET/CT-guided percutaneous liver biopsy or ablation procedures has the potential to target FDG-avid liver masses as accurately as up to 180 s breath-hold PET acquisitions.

Materials and methods

Patients

This retrospective study was conducted after local institutional review board approval and was compliant with the Health Insurance Portability and Accountability Act. Informed consent was obtained from 15 consecutive patients who underwent PET/CT-guided percutaneous interventional liver procedures using breath-hold PET/CT acquisitions, from November 2008 to December 2009. Three patients were excluded because the PET datasets were not retrievable for analysis. Two patients' liver tumours were not visible at PET and thus were excluded. The remaining 10 patients underwent fine-needle aspiration biopsy ($n = 5$), cryoablation ($n = 3$), or radiofrequency ablation ($n = 2$) procedures (Table 1). All patients had been included in one or two previous studies that described the biopsy and ablation techniques.[8,9] Thirteen liver tumours, visible on both the 180 s PET and unenhanced CT images were identified for retrospective analysis. The mean tumour diameter was 2.6 cm (range 1.2–7.1 cm; Table 1).

PET/CT technique

PET/CT images obtained at the beginning of the procedures were used for analysis. The mean intravenous FDG dose was 509.5 MBq (range 386.3–610.5 MBq); the mean uptake period was 103 min (range 78–130 min). Single bed position PET/CT images of the liver were obtained using a GE Discovery VCT 64 (GE Healthcare, Milwaukee, WI, USA). PET was obtained in two-dimensional (2D) mode as nine, 20 s, same-level breath-hold frames separated by 40 s breathing intervals. A bellows device with wireless feedback monitors (Medspira Breath Hold, Minneapolis, MN, USA) was used to facilitate same-level breath-holds for all nine PET frames and the corresponding CT acquisition.[11] Unenhanced CT was acquired using 140 kVp, 100–250 mA, and a 1.375 pitch factor. PET and CT images were reconstructed with a thickness and interval of 3.75 mm. CT attenuation correction of PET images employed the manufacturer's iterative reconstruction algorithm.

Four PET scans and one CT scan were reconstructed for each patient yielding 50 volumetric datasets. The reconstructed PET scans included 20, 40, 60, and 180 s PET acquisitions. Liver tumour conspicuity on PET was quantified as the ratio (SUVratio) of maximum pixel SUV in a region-of-interest including the entire tumour to the average SUV in a more than 1 cm^3 region-of-interest over normal liver. The mean SUVratio was 2.4 (range 1.1–6). Only the 180 s PET datasets were used during the actual PET/CT-guided interventional procedures. The 20, 40, and 60 s PET acquisitions were not used clinically but were used in this retrospective analysis.

Image analysis and statistical methods

The study readers were two abdominal radiologists, with 4–7 years of experience interpreting PET/CT and CT images and performing percutaneous image-guided liver interventions. Readers did not perform the PET/CT-guided procedures, and were not told the purpose of the study or how many subjects were involved.

Datasets were presented to the readers independently using OsiriX Advanced Open-Source PACS Workstation DICOM Viewer, version 3.5.1 (Pixmeo; Geneva, Switzerland). The PET datasets were placed in random order, followed by randomized CT datasets. Fused PET/CT images were not presented to the readers. CT images were

Table 1
Demographics and tumour characteristics of patients undergoing percutaneous positron emission tomography/computed tomography (PET/CT)-guided liver biopsies or ablations.

Patient/lesion	Age	Sex	Primary malignancy	Procedure	Liver segment(s) involved	Tumour diameter (cm)	Tumour SUVratio
1	57	F	Lung	RFA	5,6,7,8	2.9	1.8
2	53	F	Ovary	Cryoablation	4A	7.1	2.5
3	53	M	Lung Sarcoma	Biopsy	6	1.4	1.1
4/a	39	F	Breast	Biopsy	4B	1.9	2.1
4/b					8	1.2	1.2
5	40	F	Breast	Cryoablation	5,6	3.2	2.2
6	50	F	Breast	Biopsy	3	2.5	3.7
7	59	F	Colorectum	Biopsy	4A,8	2.2	2.6
8	57	M	Oesophagus	Cryoablation	2	2.4	3.2
9	52	F	Oesophagus	RFA	5,6,7,8	2.4	6.0
10/a	78	M	Colorectum	Biopsy	3	2.5	1.8
10/b					6	1.8	1.5
10/c					7	2.5	1.7

SUVratio, standardized uptake value ratio; RFA, radiofrequency ablation.

presented after PET images to decrease the likelihood of readers recognizing tumour locations from previous datasets. The readers were told how many masses to target on each dataset. Readers were instructed to scroll through each dataset and use a "point tool" to mark the geographic centre of each mass, not the most FDG-avid (PET) or solid-appearing (CT) regions. Readers were also asked to rate their confidence in targeting each tumour using a four-point scale: 0 = cannot see tumour, 1 = not confident, 2 = moderately confident, and 3 = very confident.

The three-dimensional (3D) spatial coordinates were recorded for each marked tumour on each dataset for both readers. 3D and 2D spatial differences in targeting were measured for each dataset using 180 s PET and CT as reference standards. Using 180 s PET as the standard, 20 s PET differences in targeting were compared to 40 and 60 s PET. Using CT as the standard, 20 s PET differences in targeting were compared to 40, 60, and 180 s PET.

Statistical analyses of 3D spatial differences in targeting were compared using multiple regression analysis. 2D differences were assessed for evidence of directional bias using single-sample signed rank tests in three planes. Tumour sizes and tumour SUVratio measurements were correlated with magnitudes of targeting differences and with reader confidence scores using standard Pearson correlation. All statistical tests were two-sided and $p < 0.05$ was considered significant. STATA statistical software, version 12.0 was used for all statistical tests.

Results

The magnitudes of 3D spatial targeting differences for 20 s PET, using 180 s PET as the reference standard, ranged from 0.7–20.3 mm (mean 5.3 ± 4.4 mm; median 4.3 mm) and were not statistically different to 40 and 60 s PET (Table 2). Overall differences in targeting were inversely correlated with reader confidence scores adjusted for SUV (Beta = −0.28, $p = 0.006$). Tumour size ($p = 0.001$) and tumour SUVratio ($p < 0.001$) were inversely correlated with magnitude of targeting differences.

The magnitudes of 3D spatial targeting differences for 20 s PET, using CT as the reference standard, ranged from 1.4–36 mm (mean 9.6 ± 7.1 mm; median 8.2 mm) and were not statistically different to 40, 60, and 180 s PET (Table 2). An inverse correlation of spatial differences in targeting with reader confidence scores adjusted for SUV did not achieve statistical significance (Beta = −0.14, $p = 0.16$). Tumour SUV ($p < 0.001$) was inversely correlated with magnitude of targeting differences; however, tumour size ($p = 0.16$) was not significantly correlated (Figs 1 and 2). Analysis of 2D targeting differences in the *x*, *y*, and *z* planes for both reference standards revealed no systematic directional bias (Table 3).

Discussion

A variety of imaging methods and technologies are available to the interventional radiologist. Among the newer capabilities are contrast-enhanced ultrasound and fusion technologies that can combine almost any pair of imaging techniques. PET/CT is an inherently fused imaging technology and PET/CT-guided interventional procedures are now being performed in clinical practice.[1–3] PET/CT has advantages that add substantially to the interventional radiologists' armamentarium; however, the techniques that optimize interventional PET/CT targeting are still under investigation. In the present study, single 20 s breath-hold PET acquisitions were used to target FDG-avid liver masses as accurately as up to 180 s, summed, breath-hold PET acquisitions. Spatial targeting differences were inversely correlated with the tumour SUVratio. The anticipated advantages of single breath-hold PET acquisitions for PET/CT-guided interventional procedures include reduced PET motion artefacts, improved PET/CT image registration, and shorter procedure times.

Respiratory motion artefacts and their impact on diagnostic PET images are well described and include apparent lesion elongation in directions of respiratory motion and apparent reductions in tumour SUV that decrease lesion conspicuity.[6] Respiratory motion artefacts have the

Table 2
Three-dimensional spatial differences in targeting liver masses during PET/CT-guided liver interventions, using 180 s positron-emission tomography (PET) and computed tomography (CT) as reference standards.

	Spatial differences (mm) compared to 180-S PET			Spatial differences (mm) compared to CT			
	20-S PET	40-S PET	60-S PET	20-S PET	40-S PET	60-S PET	180-S PET
Minimum	0.7	0.7	1.1	1.4	1.5	1.2	0.4
Maximum	20.3	17.3	19.0	36.0	35.7	36.8	127.3
Mean ± SD	5.3 ± 4.4	5.0 ± 3.8	5.3 ± 4	9.6 ± 7.1	9.8 ± 6.8	9 ± 6.8	12.4 ± 24.4
Median	4.3	3.5	4.5	8.2	8.4	8.4	7
p-Value[a]		0.74	0.91		0.84	0.77	0.35

SD = standard deviation, S = second.
[a] *p*-Values are compared to 20 s PET.

potential to adversely impact targeting of liver masses during interventional procedures, and can be minimized through the use of breath-hold PET acquisitions.[8,10,12,13]

Misregistration of PET/CT images produces spatial misalignment of PET and CT datasets.[7] As PET/CT guidance for interventional radiology procedures may facilitate targeting of metabolic targets not visible or poorly visible with CT and as biopsy needles and ablation applicators are typically only visible with CT and not with PET, optimal image registration during PET/CT-guided procedures is needed to assure optimal placement of devices relative to targets (Fig 1). The potential for assessing the ablation margin using PET/CT also requires optimal PET/CT image registration. Radiofrequency ablation and cryoablation do not significantly dissipate FDG activity from liver tumours.[9,14] The persistent visibility of ablated tumours on PET images at the conclusion of ablation procedures and the ability to image a sharply marginated, hypodense ice ball at unenhanced CT (when cryoablation is used) or a non-enhancing region at contrast-enhanced CT (following radiofrequency or cryoablation) allows PET/CT to be used to assess the ablation margin, assuming excellent PET/CT image registration.

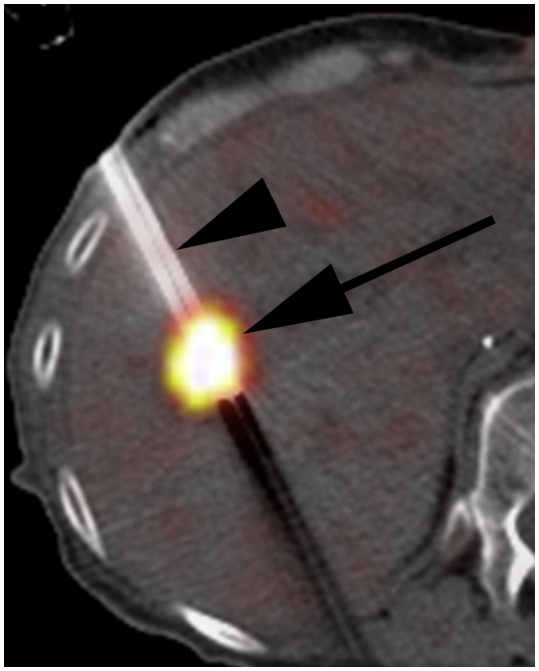

Figure 1 Fused PET/CT imaging was obtained during FDG PET/CT-guided radiofrequency ablation (RFA) of a solitary liver metastasis in a 53-year-old woman with oesophageal carcinoma. The transaxial PET/CT image was reconstructed using a 20 s breath-hold PET acquisition. The RFA applicator (arrowhead), incorporating a cluster of three internally cooled electrodes, is well-visualized on the CT image, and the tumour (arrow) is well-visualized on the PET image.

Summing nine, 20 s, same-level breath-hold PET frames and pairing the resulting 180 s PET with same-level breath-hold CT has been shown to significantly improve image registration during PET/CT-guided procedures.[8] However, acquiring multiple PET frames to generate a breath-hold PET scan is time-consuming and not always possible in sedated patients. Conversely, a single 20 s breath-hold PET frame is easier to achieve and provides good visualization of most FDG-avid tumours as demonstrated in the present study (Fig 2). Motion artefacts from a single breath-hold frame may be less pronounced than those from multiple summed breath-hold frames as even small differences in breath holding between frames may introduce artefacts.[12]

PET/CT guidance of interventional radiology procedures may include long procedure times that could negatively affect interventional radiology service workflow and the workflow or capacity of diagnostic PET/CT services. Single breath-hold PET/CT examinations may help shorten procedure times. Shorter procedures have the potential to decrease patient anaesthesia or sedation times and corresponding doses of anaesthetic drugs. Shorter procedures may also help reduce radiation exposure to personnel in the PET/CT suite. Radiation dose to personnel during FDG PET/CT-guided interventional procedures is generally well within acceptable limits and has been recently reviewed in detail.[15]

The present study has limitations. Twenty second PET acquisitions were not used intraprocedurally for targeting lesions in this retrospective study and, therefore, technical success could not be addressed; however, the images were obtained as part of a prior prospective study enabling consistent methodology of image acquisition.[8,9] The present study focused on liver masses and may not be applicable to other organs. It is noteworthy that not all liver tumours will demonstrate consistent or significant FDG uptake and that, in these situations, the 20 s breath-hold PET technique would most likely not be feasible. Readers were instructed to mark the geographic centre of masses on PET and CT images separately. As not all tumours demonstrated

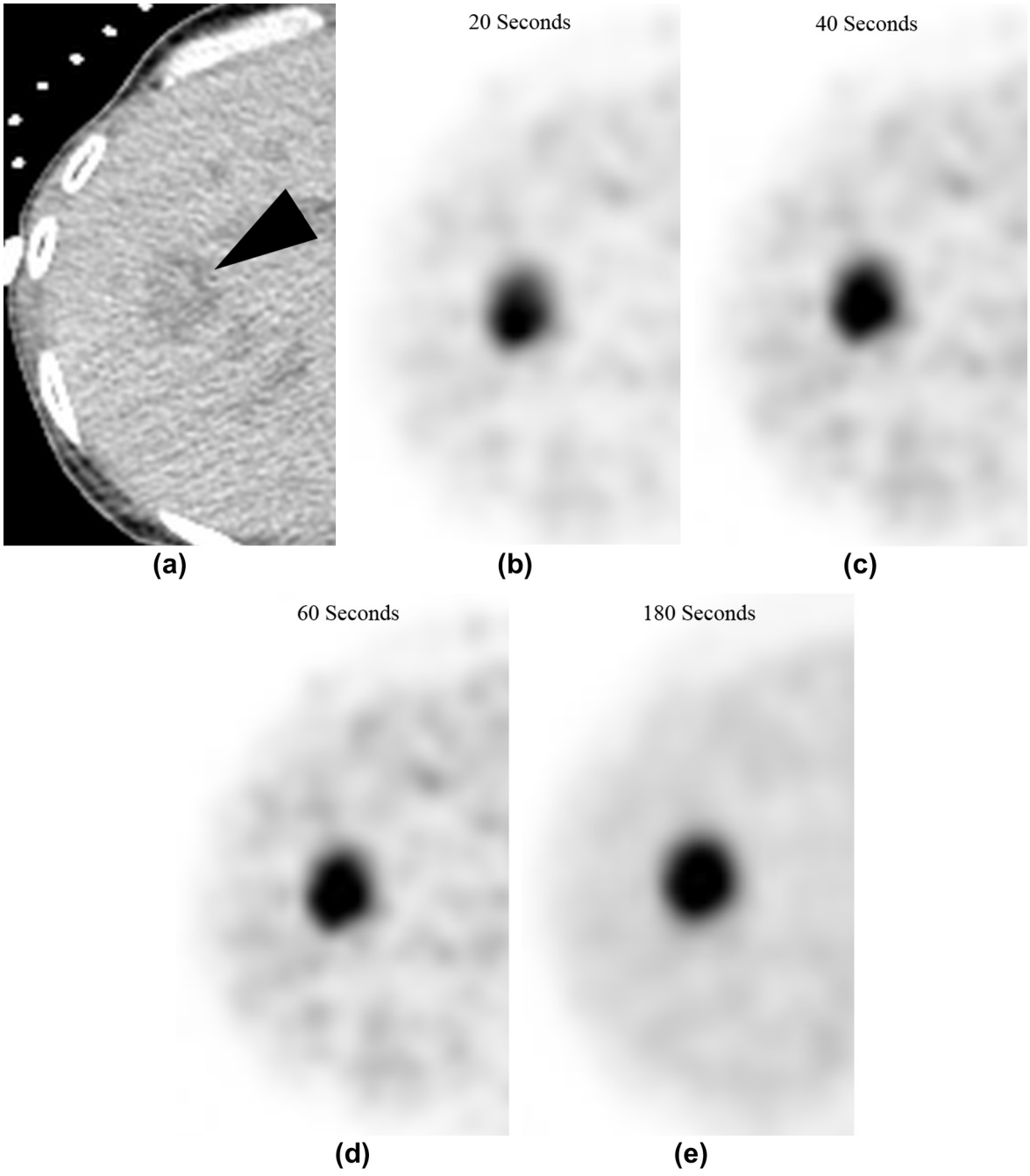

Figure 2 (a) The 2.4 cm liver metastasis (arrowhead) in the same patient shown in Fig 1 is visible on the unenhanced CT component of the PET/CT image. (b–d) The tumour has a SUV ratio of 6 and is well-visualized on the single 20 s breath-hold PET acquisition and on the summed 40, 60, and 180 s breath-hold PET acquisitions. The 20 s PET image appears noisier than the longer, summed PET acquisitions but without loss of spatial information.

Table 3
Directional bias of two-dimensional spatial differences in targeting liver masses during positron emission tomography/computed tomography (PET/CT)-guided liver interventions, using 180 s PET and CT as reference standards.

	Mean bias (mm) ± SD compared to 180-S PET			Mean bias (mm) ± SD compared to CT			
	20-S PET	40-S PET	60-S PET	20-S PET	40-S PET	60-S PET	180-S PET
X	0.1 ± 2.5 (0.92)	−0.3 ± 2.1 (0.15)	0.2 ± 2.6 (0.84)	−0.7 ± 7.0 (0.52)	−0.8 ± 6.9 (0.55)	0.2 ± 6.0 (0.55)	−5±25.7 (0.84)
Y	1.0 ± 4.9 (0.28)	0.8 ± 4.7 (0.93)	−0.2 ± 4.1 (0.06)	3.2 ± 5.0 (0.003)[a]	1.1 ± 5.7 (0.65)	0.8 ± 5.6 (0.68)	0.3 ± 4.4 (0.83)
Z	1.0 ± 3.9 (0.29)	0.7 ± 3.5 (0.35)	0.1 ± 4.6 (0.89)	−2.1 ± 7.4 (0.11)	−0.8 ± 7.9 (0.74)	−1.6 ± 7.7 (0.32)	−1.6 ± 7.1 (0.28)

SD, standard deviation; S, second. Plus or minus values refer to direction of bias. Data in parentheses are *p*-values.
[a] *p*-Value reaching statistical significance.

uniform FDG uptake on PET images and as not all tumours demonstrated uniform attenuation on CT images, the true geographic centres of tumours on PET and CT images may not have been discernable for all lesions, contributing to spatial differences in targeting. Furthermore, to enhance objectivity, readers were not presented with fused PET/CT images even though these may have enabled more precise recognition of tumour morphology and geometric centres. Large spatial differences in targeting for two lesions appeared to have been related to misidentification of lesions that would not have occurred if readers had been provided fused PET/CT datasets. However, the method was selected to enable objective comparison of the targeting performance of variable duration PET acquisitions and not to optimize targeting in a prospective procedural setting. A larger study would have been required to determine minimum tumour size and SUV cut-off values for the use of 20 s breath-hold PET acquisitions during PET/CT-guided interventions. The present study was conducted using a combined PET/CT machine with bismuth germanium oxide PET detector materials. Newer PET/CT machines commonly incorporate lutetium orthosilicate or similar detector materials that enable shorter PET acquisition times.[16] Accordingly, less than 20 s PET acquisitions may be feasible in the future.

In conclusion, single 20 s breath-hold PET acquisitions from PET/CT-guided percutaneous liver procedures have the potential to target FDG-avid liver masses with equivalent accuracy to 180 s summed, breath-hold PET acquisitions and may facilitate strategies that improve image registration and shorten procedure times.

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