Technical Note: Scintillation well counters and particle counting digital autoradiography devices can be used to detect activities associated with genomic profiling adequacy of biopsy specimens obtained after a low activity ^{18}F -FDG injection

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Purpose: Genomic profiling of biopsied tissue is the basis for precision cancer therapy. However, biopsied materials may not contain sufficient amounts of tumor deoxyribonucleonic acid needed for the analysis. We propose a method to determine the adequacy of specimens for performing genomic profiling by quantifying their metabolic activity.

Methods: We estimated the average density of tumor cells in biopsy specimens needed to successfully perform genomic analysis following the Memorial Sloan Kettering Integrated Mutation Profiling of Actionable Cancer Targets (MSK-IMPACT) protocol from the minimum amount of deoxyribonucleonic acid needed and the volume of tissue typically used for analysis. The average ^{18}F -FDG uptake per cell was assessed by incubating HT-29 adenocarcinoma tumor cells in ^{18}F -FDG containing solution and then measuring their activity with a scintillation well counter. Consequently, we evaluated the response of two devices around the minimum expected activities which would indicate genomic profiling adequacy of biopsy specimens obtained under ^{18}F -FDG PET/CT guidance. Surrogate samples obtained using 18G core needle biopsies of gels containing either ^{18}F -FDG-loaded cells in the expected concentrations or the corresponding activity were measured using autoradiography and a scintillation well counter. Autoradiography was performed using a CCD-based device with real-time image display as well as with digital autoradiography imaging plates following a 30-min off-line protocol for specimen activity determination against previously established calibration.

Results: Cell incubation experiments and estimates obtained from quantitative autoradiography of biopsy specimens (QABS) indicate that specimens acquired under ^{18}F -FDG PET/CT guidance that contained the minimum amount of cells needed for genomic profiling would have an average activity concentration in the range of about 3 to about 9 kBq/mL. When exposed to specimens with similar activity concentration, both a CCD-based autoradiography device and a scintillation well counter produced signals with sufficient signal-to-background ratio for specimen genomic adequacy identification in less than 10 min, which is short enough to allow procedure guidance.

Conclusion: Scintillation well counter measurements and CCD-based autoradiography have adequate sensitivity to detect the tumor burden needed for genomic profiling during ^{18}F -FDG PET/CT-guided 18G core needle biopsies of liver adenocarcinoma metastases. © 2018 American Association of Physicists in Medicine [https://doi.org/10.1002/mp.12836]

Key words: autoradiography, beta particles, biopsy, FDG PET, scintillation cameras

1. INTRODUCTION

Core needle biopsy of tumors is a pivotal tool for cancer diagnosis and its accuracy is dependent on the correct placement of the biopsy needle in the tumor. The use of PET/CT guidance is of growing importance for interventional procedures¹ and several studies^{2–7} report that it has potential for improving targeting and diagnostic efficiency. It has also been shown that injecting the patient with 2-deoxy-2-(^{18}F)fluoro-D-glucose (^{18}F -FDG) prior to a core biopsy procedure (i.e., harvesting of small cylinders of tissue) and then measuring the activity distribution along the specimen using autoradiography (ARG) can provide information about the metabolic activity within the specimen with a spatial resolution much higher than that of PET.⁸ The potential uses of this approach span across various oncologic applications including the evaluation of the adequacy of the specimen for diagnosis, *in situ* evaluation of new PET tracers, guidance and improvement of the sensitivity of histopathology analysis as well as tumor margin evaluation. Here, we show the feasibility of autoradiography of biopsy specimens obtained under PET/CT guidance for another increasingly important characterization: their adequacy for genomic profiling.

Genotype-directed therapies have been shown to prolong median survival of patients with metastatic melanoma⁹ and metastatic lung adenocarcinoma.¹⁰ Despite this promise and that of other potential driver mutation-based therapy approaches,¹¹ genomics-driven oncology is facing a number of challenges, one of which is the efficient collection of sufficient amounts of deoxyribonucleonic acid (DNA) material from small tissue samples such as image-guided biopsies.¹² For example, the low prevalence of some rearranged during transfection (RET) mutations have caused 10.7% failure rate in immunohistochemistry (IHC) analysis “largely due to an inadequate number of tumor cells in the samples” and 26.9% failure rate in fluorescence *in situ* hybridization (FISH) analysis “largely due to an inadequate number of tumor cells or sample quality”.¹³ Memorial Sloan Kettering Integrated Mutation Profiling of Actionable Cancer Targets (MSK-IMPACT)^{14,15} performs high throughput profiling of DNA alterations in key cancer genes observed in samples from solid tumors and is also facing limitations due to “insufficient tumor content (n = 328; 3%) or DNA yield (n = 793, 6%)” as found in a cohort of more than 10,000 cases.¹⁵ In addition, biopsy diagnostic sensitivity alone can also vary between about ~30% and ~95% depending on cancer type and location, image guidance, and the use of on-site cytopathology evaluation.^{16–18}

Repeating the diagnostic interventional procedures for nondiagnostic/insufficient biopsy specimens has been associated with increased risks, psychological burden, and costs for the patient and leads to delay in rendering the final molecular diagnosis. Therefore, performing the proposed biopsy specimen evaluation method while the patient is still in the interventional suite may help improve the efficacy of the diagnostic procedure, and so ensure prompt delivery of precision therapy to a larger number of cancer patients in a timely manner. In this technical note is shown that it is feasible to measure the ^{18}F -FDG activity corresponding to the minimum average amount of DNA needed for genomic profiling, so that the interventional radiologist can be immediately notified if further tissue extractions are needed while the patient is still on the operation table.

2. MATERIALS AND METHODS

The feasibility of the method is shown following these steps: (a) estimation of the minimum average density of tumor cells which would render a specimen adequate for genomic profiling; (b) measurement of the ^{18}F -FDG uptake per cell *in vitro* under conditions similar to those *in situ* and calculation of the specimen activity corresponding to the required amount of DNA; (c) preparation of surrogate specimens containing ^{18}F -FDG-loaded tumor cells or specific activity derived from (a) and (b); and (d) performing autoradiography and activity measurements of the surrogate specimens using different techniques as described below.

2.A. Estimation of the average tumor cell density required for genomic-profiling adequacy and the respective ^{18}F -FDG uptake per cell

The number of cells required for the MSK-IMPACT genomic analysis can be obtained by dividing the amount of DNA needed (10^5 ng) by the average amount of DNA per cell (~6 ng), yielding $\sim 1.7 \cdot 10^4$ cells. This amount of DNA is typically found in about 20 sections of core needle biopsies each with 10 μm thickness. For a 10-mm long specimen extracted with 18G core biopsy needle (specimen diameter ~0.8 mm) and assuming a uniform tumor cell distribution, this number of tumor cells is found in about 1.6 mm^3 (μL) of tissue-yielding tumor cell density of $\sim 10^4$ tumor cells per μL . We use this number as an estimate of the average minimum tumor cell density across tumors needed for harvesting sufficient amount of DNA in the typically analyzed amount of tissue.

The ^{18}F -FDG uptake for adenocarcinoma liver metastasis can be roughly estimated from measurements of the activity of biopsy specimens in a previous investigation.⁸ Autoradiography of the PET/CT-guided biopsies in our institution was performed between 65 min and ~4 h after the injection with mean of ~2 h, excluding few postablation cases,⁶ for which the ARG measurements were performed within less than 25 min after a second FDG injection. From the 19 biopsy pieces investigated in that study, specimens were found to be positive with probability greater than 75% if their measured SUV_{ARG} was larger than ~7. SUV_{ARG} is obtained from the specimen activity as measured by autoradiography divided by the injected activity normalized the patient weight.⁸ For a 70-kg patient injected with the mean activity for these procedures of 200 MBq (5.4 mCi) ^{18}F -FDG, the specimen-specific activity corresponding to this SUV_{ARG} threshold would be 9 kBq/mL ~2 h post injection. Using an estimate for the tumor cell density of $\sim 10^4$ tumor cells per μL and the definition of activity, this gives about 8.5 ^{18}F -FDG molecules average minimum uptake per cell at time of ARG for diagnostically adequate specimens. Ten times higher tumor cell concentration would reduce that estimate to 0.85 ^{18}F -FDG molecules per cell.

2.B. Incubation of cells with FDG

We have performed two types of experiments, which involved incubation of cells with ^{18}F -FDG: (a) for determining cell uptake and (b) for incorporation of cells loaded with FDG in the surrogate specimens. Since in our institution, the largest number of PET/CT-guided biopsies is performed for colorectal adenocarcinoma metastasis in the liver, a human colorectal adenocarcinoma cell line HT-29 was selected for this investigation. Cells were incubated with ^{18}F -FDG to determine ^{18}F -FDG uptake per cell as a function of incubation time. HT-29 cells were seeded in six-multiwell plates 48–72 h before incubation. About 53 kBq/mL ^{18}F -FDG in 2 mL of incubation buffer was added to each culture well. The glucose concentration of the incubation buffer was 5.5 mmol/L. The incubation was stopped by removing the incubation buffer from the wells and rinsing the wells twice with phosphate-buffered saline (PBS). The incubation time was varied from 15 to 75 min with a 15-min step. After incubation, the cells from one well were removed from the incubation flask by soaking them for few minutes in trypsin. The cells were then separated from the supernatant (liquid portion remaining after precipitation of the cells component) by centrifuging after which they were counted using a hemocytometer (a glass slide with an etched grid and a known volume to facilitate cell counting). In the other wells, the cells were dissolved using NaOH and removed from the well for radioactivity measurement with a scintillation well counter (1282 CompuGamma Gamma counter CS, LKB Wallac, 3" $\times$ 3" NaI (TI) well type crystal) for 1 min. The experiment was repeated three times to obtain the average uptake.

In a second experiment, cells were incubated with ^{18}F -FDG to produce surrogate specimens using ^{18}F -FDG containing cells embedded in gel specimen models. In

this experiment, HT-29 colorectal adenocarcinoma tumor cells were incubated in ^{18}F -FDG containing solution (activity concentrations = 1.51 MBq/mL and glucose concentrations of 16.5 mmol/L) for 65 min. After that, the cells were separated from the supernatant and counted as described above and added to the gelatine mixture described below.

2.C. Surrogate specimen preparation

To measure the autoradiography and scintillation well counter signal from surrogate biopsy specimens with realistic tumor cell and activity concentration, surrogate gels containing activity similar to that in actual tissue specimens were prepared in two different ways.

2.C.1. Adding ^{18}F -FDG to the gels

In the first approach, ^{18}F -FDG activity was added to a pre-heated mixture containing gelatin (5 g), glycerol (30 g), water (15 g), and a small amount of a violet dye (<0.1 g Crystal Violet C581, Fisher Scientific) as previously described.⁸ The mixture was then refrigerated at 4°C for 1 h and the cold gel was then biopsied using 18G core biopsy needles. The resulting gel has atomic composition similar to that of tissue¹⁹ and density of about 1.2 g/cm³. The average thickness of the surrogate specimens was measured by scanning fluorescent microscopy (using Leica SP5 inverted laser scanning microscopy employing broad visible emission spectrum of the dye and 488 nm laser for excitation) to be between 0.4 and 0.5 mm. This is similar to the average thickness of patient biopsy specimens obtained with 18G core needles after the slide is turned over and they are compressed by the weight of the slide (~0.4 mm).

Monte Carlo simulations using the GATE Monte Carlo code^{20,21} were performed to determine the error introduced using the above gelatin mixture as an approximation to tissue in the experiments. The geometry shown in Fig. 1 was simulated for the materials described above with 2×10^6 histories originating from the ^{18}F general purpose source which accounts for the positron energy distribution. The simulation parameters used were standard physics model with positron annihilation and multiple scattering, 2.2 μm range cuts for positrons and electrons and 0.1 keV minimum energy cut. Allowing production of positrons and electrons above such low energies²⁰ was selected in view of the small thickness of the detector layers (Fig. 1).

The energy deposited in the phosphor layer of an autoradiography plate from 0.4 to 0.5 mm thick specimen models placed on top of the plate showed about 4.4% less energy deposited from such gel mixture sample when compared to liver and spleen models.¹⁹ Therefore, determining the absolute activity of liver specimens using a calibration curve derived using this gel mixture⁸ with higher accuracy would require reducing the ARG signal obtained from the specimen by ~4.4% prior to using the calibration equation.

FIG. 1. A schematic (not to scale) and thicknesses of the biopsy imaging plate measurement components used to simulate the autoradiography process. Two biopsy samples with 0.4 and 0.5 mm width and 19 and 16 mm length were simulated on top of an imaging plate model.¹⁹ [Color figure can be viewed at wileyonlinelibrary.com]

2.C.2. Adding ^{18}F -FDG-loaded cells to the gels

In this second approach, we added ^{18}F -FDG-loaded HT-29 cells instead of FDG to the gels described above. The cells were incubated with ^{18}F -FDG and then separated from the supernatant as described in Section 2.B. The number and the concentration of the cells in the surrogate gelatin specimens were determined after staining with a pan-nuclear marker that dyes all nuclei (DAPI), using a Zeiss LSM 5Live line scanning confocal microscope.

The activity concentration of the FDG gel surrogate specimens (Section 2.C.1 above) was obtained by measuring the activity and weight of five larger samples (between 0.2 and 0.7 g) from different parts of the gel. The variation in the activity concentration between these samples was <2%. This specific activity was later used as the basis for the calibration curve shown in Fig. 4.

2.D. Autoradiography and scintillation well counter measurements

As a digital autoradiography device,²² we used the Micro Imager (Biospace Lab S.A., Paris, France). Exposures were 20 min each and the counts were accumulated in list mode format (which records the time for each particle interaction in addition to its coordinates) allowing to test the quality of images with arbitrarily shorter exposure times. The response of the Micro Imager was calibrated using surrogate samples with activity concentrations around the estimate of the minimum average activity of specimens containing colorectal adenocarcinoma tumor cells by measurements for activity concentrations between ~0.5 and 50 kBq/g, which would translate to about

0.6 and 60 kBq/mL of the gel. Three samples were measured consecutively until the activity decayed to about 3.5 kBq/mL. Although this activity concentration roughly corresponds to the minimum adequate amount of tumor cells, one of the samples was measured overnight for 10 h in order to perform measurements for activities decaying down to the minimum activity resolvable in the ARG images.

To investigate system performance for shorter exposures, 3, 5, and 10 min subsets were extracted from the beginning of each 20-min exposure. A photograph at fixed distance was used to produce a contour (mask) of the specimen which was manually registered with the ARG image. The number of counts within this contour for 10-min exposures was used to build a calibration curve. From the list mode file of the last 10-h long exposure, 10-min exposures were extracted at several different times until the sample ARG image could no longer be resolved from the background.

Autoradiography with digital autoradiography (DAR) imaging plates (Fujifilm BAS-MS 2025) was obtained by exposing the plates to the specimen in a dark enclosure for 10 min and scanning the plates 20 min after the end of exposure by a Typhoon FLA 7000 scanner (GE Healthcare, Little Chalfont, UK) with a 632 nm laser.⁸

For the gels loaded with cells, after performing the ARG measurements, the surrogate samples were removed from the slides and measured with a scintillation well counter as described in Section 2.B. The activity of all rinsing solutions was also measured for ^{18}F -FDG uptake verification.

3. RESULTS

3.A. ^{18}F -FDG uptake per cell and ^{18}F -FDG concentrations

The results from the experiments for determining the ^{18}F -FDG uptake per cell as a function of time are summarized in Fig. 2.

This group of incubation experiments yields an uptake of about 2.9 ± 0.8 ^{18}F -FDG molecules per cell at end of 1-h incubation. For 10^4 tumor cells per μL , this would give 3 kBq/mL.

The 65-min incubation of cells from the second type of experiments (see Section 2.B), which were later mixed in a

FIG. 2. Plot of the number of ^{18}F -FDG molecules per HT-29 tumor cell as averaged from three measurements at the end of 15, 30, 45, 60, and 75 min incubation in 53 kBq/mL ^{18}F -FDG solutions with glucose concentration of 5.5 mmol/L.

FIG. 3. Autoradiography (ARG) images of a surrogate ^{18}F -FDG-loaded HT-29 adenocarcinoma cells. ARG images obtained using the Micro Imager for 5-, 10-, and 20-min exposures and with the Fujifilm digital autoradiography (DAR) imaging plate for 10 min with gel activity concentrations at the start of exposure of ~ 1.3 and ~ 1.5 kBq/mL, respectively.

surrogate gel yielded 4.5 ± 0.4 ^{18}F -FDG mol/cell at the end of incubation. After adding these cells to the gel (concentration of 3.62×10^7 cells/mL), the concentration of ^{18}F -FDG molecules in the surrogate biopsy specimens at the time of autoradiography with the Micro Imager (3.5 h later) resulted in about 4.4×10^7 molecules ^{18}F -FDG/mL or 4.6 kBq/mL.

3.B. Sensitivity and calibration of a CCD based device

Figure 3 shows ARG images of the surrogate specimen containing FDG-loaded HT-29 cells obtained using the Micro Imager for different exposure times and a Fujifilm DAR imaging plate. The surrogate specimen is loaded with 3.62×10^4 HT-29 adenocarcinoma cells per microliter containing 1.2 and 1.4 ^{18}F -FDG molecules per cell at the start of

exposure of the Micro Imager and the Fujifilm DAR plates, respectively.

Figure 4 shows the calibration curve for the Micro Imager, based on surrogate specimens obtained by performing biopsy of the gels directly loaded with the expected activity concentrations with 18G core needles. The specific activity is calculated for the midpoint of the 10-min exposures, so that the image frame decay correction is less than 1% and can be neglected.²³ The scatter of points for specific activities above about 3 kBq/g reflects both a variation in the thicknesses of the three samples used and in the accuracy of aligning the specimen mask with the autoradiography image. Since only one sample was used for activities lower than 3 kBq/g, the scatter of points in that region is due only to the variations in the mask aligning accuracy.

The ARG images (Fig. 3) and the calibration curve (Fig. 4) show the ability of the Micro Imager to reliably measure the activity in biopsy specimens with specific activities down to ~ 1 kBq/g which is below the expected activity range (~ 3 to ~ 9 kBq/mL) corresponding to the minimum amount of tumor cells needed for genomic-profiling adequacy according to Sections 3.A and 2.A. Using this calibration curve for liver specimens would require applying a density difference correction as discussed in Section 2.C.

3.C. Well counter measurements

Scintillation well counter measurements were performed for a surrogate specimen loaded with HT-29 cells after incubation with ^{18}F -FDG. A measurement performed at the end of the day after all other measurements (6:36 h after the end of incubation) yielded 75 cpm which was 20.8 times higher than the 3.6 cpm background. This corresponds to activity of 3.6 Bq or about $1.34 \text{ Bq}/\mu\text{L}$ for this $2.72 \mu\text{L}$ volume surrogate specimen. Such activity concentration is about 13% lower than the specific activity obtained from the DAR imaging plate for the

FIG. 4. Calibration curve for the Micro Imager at low-specific activities built using surrogate samples obtained with an 18G core biopsy needle and 10-min exposures. The presented error bars for the points above 3 kBq/g reflect errors introduced by both variation in the thickness of different samples ($\sim 15\%$) and by the uncertainty in registering the specimen contour (or mask) with the autoradiography image ($\sim 2\%$). The error bars for the points below 3 kBq/g reflect only the latter. [Color figure can be viewed at wileyonlinelibrary.com]

same specimen. The difference could be due to loss of activity in the process of transferring a very small amount of gel from the slide to the counting vial (Eppendorf tube).

4. DISCUSSION

We measured the average ^{18}F -FDG uptake per cell for adenocarcinoma liver cells at the end of incubation to be between about 2 and about 5 ^{18}F -FDG molecules per cell from two *in vitro* incubation experiments. From human specimens at the average time for performing autoradiography, which is ~ 2 h post injection, we obtained expected minimum number of ^{18}F -FDG molecules per cell ranging from 0.85 to 8.5 depending on whether the tumor cell concentration is assumed to be 10^5 or 10^4 cells/ μL , respectively. A difference between the *in vitro* and *in situ* uptake values is expected due to: (a) difference in the uptake time: ~ 1 h for the *in vitro* and ~ 2 h for the *in situ* cells; (b) difference in the incubation conditions between *in vitro* and *in situ*, which will be affected by tumor vascularity, glucose concentration, etc.^{24,25} Longer incubation leads to higher uptake as shown in Fig. 2, but that effect is soon offset by isotope decay. Using an estimate of the tumor cell density of 10^4 μL^{-1} , we conclude that the minimum expected specific activity for rendering typical biopsy specimens from colorectal adenocarcinoma metastases in the liver as adequate for genomic profiling would be between about 3 and about 9 kBq/mL.

Reducing the uncertainty of this estimate requires further investigations. Since the specific activities of the biopsy specimens will be affected by variations in the injected activity, the time of measurement, and the patient body habitus, the genetic-profiling adequacy threshold will be searched for in units of SUV_{ARG} , similar to the diagnostic adequacy threshold previously established.⁸ In analogy with that work, the threshold for genomic-profiling adequacy will have certain confidence limits due to perturbing metabolic phenomena like inflammation. Applying a correction for the lean body mass of the patient²⁶ may further reduce the uncertainty of the threshold.

The above discussion is based on the average FDG uptake per cell values as determined from 19 cases and from *in vitro* experiments. As discussed above, due to variable *in situ* conditions, the uptake per cell may vary. This may produce a variation in the number of cells corresponding to the same specimen activity. Measuring uptake per cell in a series of clinical cases may indicate how such variation will affect the confidence limits for the potential specimen activity threshold for genomic-profiling adequacy. This can be accomplished by measuring the activity of the biopsy specimens and also by counting the tumor cells in them.

Furthermore, we tested the performance of an existent CCD-based device and a scintillation well counter using surrogate specimens with activities around the lower specific activity limits indicated above. We showed that these devices have sufficient sensitivity and signal-to-noise ratio to test the genomic-profiling adequacy of adenocarcinoma liver biopsy specimens. In our experiments, the ^{18}F -FDG-loaded cancer cells and the ^{18}F activity were uniformly distributed in the surrogate gels. If the tumor cells are nonuniformly

distributed, the ARG signal will be stronger and therefore more easily identifiable in the areas of higher tumor cells concentration; however, regions with specific activity lower than the ARG detection threshold will be missed, which may result in slight underestimation of the specimen activity.

On the other hand, the count rate from the scintillation well counter will be averaged over the whole specimen and will provide more accurately the activity of the entire specimen; however, small pockets of activity may not bring the signal above a diagnostic adequacy threshold. Therefore, false-negative predictions may occur with both methods for tumors with high degree of nonuniformity of the tracer uptake. Clearly, due to differences between the different types of tumor tissue, further investigations of the diagnostic and genomic-profiling adequacy of biopsies of different tumors using both methods in conjunction with cytology evaluation and tumor cell counting are needed. Cell counting is needed since cytology analysis can help answer the diagnostic adequacy question, but it cannot answer the genomic-profiling adequacy question.

Inflammation can also lead to an increased FDG uptake. However, performing a biopsy of a lesion which is FDG avid due to inflammation will still result in diagnosis. Potentially problematic could only be cases where inflammation is present in a tumor. For example, that may occur after radiation therapy. However, in most diagnostic settings, this is not a big factor. From 45 cases for which we performed quantitative autoradiography of biopsy specimens (QABS) measurements, we had only one mesenteric lymph node biopsy in which FDG uptake was correlated to inflammation, there were no tumor cells in the measured specimen, and the histopathology diagnosis based on all specimens was negative.

Therefore, injecting the patient with a small (<222 MBq or 6 mCi) amount of ^{18}F -FDG is expected to facilitate a reduction in the number of needle insertions and result in decreasing the probability for requesting a repetition of the biopsy procedure. This would reduce the risks for the patient associated with repeating the biopsy,²⁷ make precision therapy available to more patients, and can lead to significant cost savings. These benefits are expected to outweigh the risk from the associated radiation dose which is less than half of that from a diagnostic PET scan. The effective dose to the patient from half of the standard diagnostic 444 MBq (12 mCi) ^{18}F -FDG injection is $6 \text{ mCi} \times 37 \text{ MBq/mCi} \times 0.019 \text{ mSv/MBq} = 4.2 \text{ mSv}$.²⁸ This is less than twice the average annual effective dose from natural sources (2.4 mSv/a).²⁹ The doses to the personnel from standard ^{18}F -FDG injections, which contain twice higher activities (444 MBq), were previously found not to be significantly higher than the doses from fluoroscopically guided procedures.³⁰ For this reason, further validation of this technique could justify extending metabolic activity-based biopsy guidance to different tumor types and implementing it in small practices which do not possess a PET/CT scanner dedicated for interventional procedure guidance. If only specimen autoradiography is used for guidance of biopsies of ^{18}F -FDG avid lesions instead of CT or PET/CT guidance (~ 24 mSv CT only dose),^{31,32} the effective dose to the patient from the procedure will be reduced about six times. With further research the

method can be extended to other PET tracers as well as to several non-PET radiopharmaceuticals.

5. CONCLUSION

Scintillation well counter measurements and CCD-based autoradiography have adequate sensitivity to detect the tumor burden needed for genomic-profiling during 18G core needle biopsy procedures for FDG PET avid tumors in patients injected with a small amount of ^{18}F -FDG activity before the biopsy. A fast dedicated QABS imager based on particle counting, with sensitivity achievable by today's standards, is expected to have an advantage in determining the diagnostic adequacy of the biopsy due to positional mapping of the activity distribution along the specimens. Performing such measurements could significantly increase the efficiency of biopsy procedures for molecular cancer diagnosis and may allow providing precision therapy to more cancer patients.

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CONFLICT OF INTEREST

The authors have no conflicts to disclose.

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