Novel Method to Detect and Characterize ^{18}F-FDG Infiltration at the Injection Site: A Single-Institution Experience

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A novel quality control and quality assurance device provides time–activity curves that can identify and characterize PET/CT radiotracer infiltration at the injection site during the uptake phase. The purpose of this study was to compare rates of infiltration detected by the device with rates detected by physicians. We also assessed the value of using the device to improve injection results in our center. **Methods:** 109 subjects consented to the study. All had passive device sensors applied to their skin near the injection site and mirrored on the contralateral arm during the entire uptake period. Nuclear medicine physicians reviewed standard images for the presence of dose infiltration. Sensor-generated time–activity curves were independently examined and then compared with the physician reports. Injection data captured by the software were analyzed, and the results were provided to the technologists. Improvement measures were implemented, and rates were remeasured. **Results:** Physician review of the initial 40 head-to-toe field-of-view images identified 15 cases (38%) of dose infiltration (9 minor, 5 moderate, and 1 significant). Sensor time–activity curves on these 40 cases independently identified 22 cases (55%) of dose infiltration (16 minor, 5 moderate, and 1 significant). After the time–activity curve results and the contributing factor analysis were shared with technologists, injection techniques were modified and an additional 69 cases were studied. Of these, physician review identified 17 cases (25%) of infiltration (13 minor, 3 moderate, and 1 significant), a 34% decline. Sensor time–activity curves identified 4 cases (6%) of infiltration (2 minor and 2 moderate), an 89% decline. **Conclusion:** The device provides valuable quality control information for each subject. Time–activity curves can further characterize visible infiltration. Even when the injection site was out of the field of view, the time–activity curves could still detect and characterize infiltration. Our initial experience showed that the quality assurance information obtained from the device helped reduce the rate and severity of infiltration. The device revealed site-specific contributing factors that helped nuclear medicine physicians and technologists customize their quality improvement efforts to these site-specific issues. Reducing infiltration can improve image quality and SUV quantification, as well as the ability to minimize variability in a site's PET/CT results.

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With the commercialization of the first PET/CT scanner in 2001, this technology has played an ever-increasing role in oncology, neurology, cardiology, and various other applications. ^{18}F-FDG PET is used to diagnose, stage, and restage many cases of cancer. Accuracy ranges from 80% to 90% and is often better than that of anatomic imaging (*1–3*). Since changes in ^{18}F-FDG accumulation have been shown to be useful as an imaging biomarker for assessing response to therapy, PET/CT scanning through this combination of molecular and anatomic imaging is playing an ever-increasing role in quantitatively measuring individual response to therapy and even in evaluating new drug therapies (*4,5*).

The SUV is commonly used as a relative measure of labeled radiotracer uptake indicating the amount of cellular activity occurring. The SUV is a ratio of the radioactivity concentration in an area of interest to the decay-corrected amount of radiolabeled tracer divided by the subject's weight in grams. It is believed that the 2 largest factors that influence SUV are injected dose and subject size (*5*). Primary factors that affect the delivered dose of ^{18}F-FDG include the uptake duration between injection and scan, residual syringe activity measurement, dose infiltration near the injection site, subject weight measurement, clock synchronization for measuring dose assays and scanning, and data entry. Infiltration is a common problem that can occur when the radiolabeled tracer infuses the tissue near the venipuncture site and can result from the tip of the catheter slipping out of the vein or passing through the vein. Additionally, the blood vessel wall can allow part of the tracer to infuse the surrounding tissue. Therefore, infiltration has the potential to underestimate the metabolic activity of lesions and internal reference points, which can affect the interpretation of the study. Although there is very little published information on ^{18}F-FDG infiltration rates, they are not insignificant and the impact on SUV is not fully characterized.

This study applied a novel quality control device, Lara (provided by Lucerno Dynamics, LLC), which uses time–activity

curves to dynamically characterize the quality of an ^{18}F injection during the uptake period. The study aimed to compare physician-review results for standard clinical PET images with device-sensor results for infiltration detection and characterization. When we noted initial high infiltration rates, we expanded the scope of the study. Contributing factors were analyzed and shared with technologists, improvements to practice patterns were implemented, and rates were remeasured.

MATERIALS AND METHODS

Patients

The study was approved by our institutional review board at Saint Louis University, and all subjects signed an informed consent form. The study was also registered with Clinicaltrials.gov (identifier NCT03041090). Subjects were identified once they arrived for their standard-of-care PET/CT examination and were asked about their interest in participating. If interested, an informed consent dialogue occurred between the subject and the engaged team member, such as a PET technologist, physician, or research coordinator. The informed consent document was signed by the subject and retained by the research team.

Sensor Application and PET/CT Scanning

Once consent was obtained, the subject continued with the standard-of-care screening process. A Lara device, consisting of 2 scintillation sensors, 2 pads, a reader, and a docking station, was available in each uptake room. Just before the ^{18}F-FDG injection, the sensors were placed by the PET/CT technologist on the subject (injection site and contralateral arm; Fig. 1). The sensors remained in place for the ^{18}F-FDG uptake period (typically 60–90 min) while the subject sat in a reclined chair. Afterward, the sensors were removed by the technologist. The subject then underwent true whole-body static PET/CT imaging from head to toe, which is the standard of care at our institution for all cancer patients. PET/CT images were acquired about 70 min after injection. Participation in the study did not cause the subject to receive additional radiation, and use of the device added only 1 min to the time of the PET/CT examination. The study team then uploaded the sensor data for each injection to the personal computer in the PET/CT control room. The team also uploaded other factors, such as the injection location and orientation; needle gauge; injecting technologist name; radiotracer type and dose; and subject height, weight, and glucose level. Data were then transferred via the Internet to Lucerno Dynamics and were automatically analyzed. After undergoing imaging, the subject was asked to complete a brief survey on the comfort of the Lara device. This coded paper survey was submitted to Lucerno Dynamics for further development of the device.

Data Analysis

Two board-certified nuclear medicine physicians reviewed the PET/CT images for any evidence of uptake at the site of injection and reported their findings. Time–activity curves generated from the applied sensors were independently examined and then compared with the physician reports. Time–activity curve information was recorded along with physician-report information, and differences between the two were documented.

After data had been obtained for the initial 40 subjects, a contributing factor analysis was done and the results shared with the technologists. Improvement measures were implemented, after which infiltration rates were measured in the next 69 subjects.

FIGURE 1. (Top) Sensors placed on injection arm and contralateral control arm. (Bottom) Lara device consists of 2 scintillation sensors, 2 pads, a reader, and a docking station.

RESULTS

Physician review of images for the initial 40 subjects (undergoing standard clinical-image uptake processes) found visible evidence of infiltration in 15 (38%). Sensor time–activity curves for the same 40 subjects identified infiltration in 22 (55%). Of these 40 subjects, 20 were injected in the right arm and 20 in the left arm. The rate of infiltration was 40% (8/20) on the right and 70% (14/20) on the left. Of the right-sided infiltrations, 2 of 13 (15%) were injections at the antecubital fossa and 6 of 7 (86%) were injections distal to the antecubital fossa. Of the left-sided infiltrations, 0 of 1 (0%) were injections proximal to the antecubital fossa, 3 of 7 (43%) were injections at the antecubital fossa, and 11 of 12 (92%) were injections distal to the antecubital fossa. Figure 2 depicts time–activity curves obtained from sensor recordings for 3 subjects. These results are reviewed in Tables 1 and 2.

Time–activity curve results and the contributing factor analysis were shared with the technologists injecting the radiotracer. After the injection technique had been modified, physician review of images for the next 69 subjects (undergoing standard clinical-image uptake processes) found visible evidence of infiltration in 17 (25%). Sensor

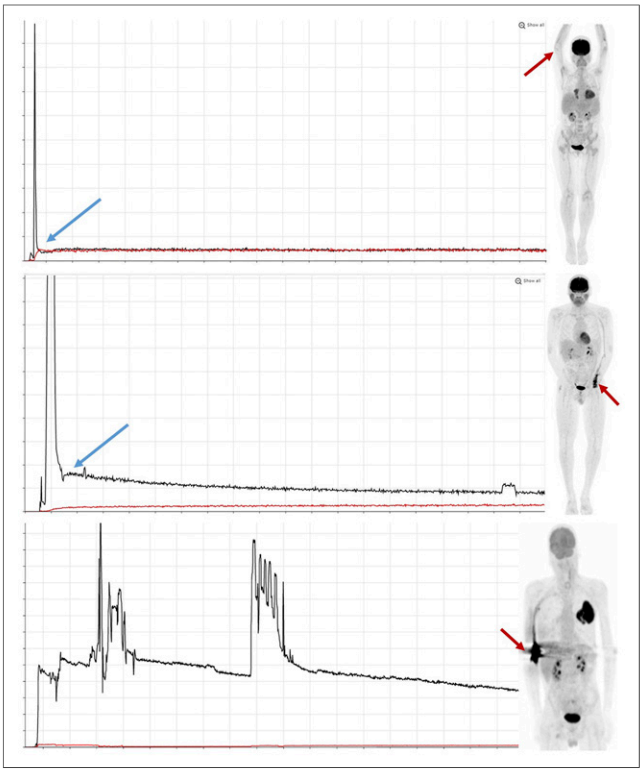

FIGURE 2. Time–activity curves from sensor recordings in 3 subjects. (Top) Example of ideal injection in right antecubital fossa. Sensor results drop immediately to reference arm level. (Middle) Example of moderate infiltration with injection in left wrist. Sensor results do not drop immediately to reference arm level. (Bottom) Example of severe infiltration with injection in right antecubital fossa. Sensor results never fall to reference arm level. Red line = reference arm level; red arrow = injection site; black line = sensor result; blue arrow = drop in sensor result.

time–activity curves for the same 69 subjects identified infiltration in 4 (6%). These results are reviewed in Table 3.

DISCUSSION

The most commonly used injection site for PET/CT examinations is the antecubital fossa, with other injection sites being more distal on the arm. Most patients are imaged from the base of the skull to the upper thighs with the arms up (*6*). Studies that have reviewed injection site images have shown that dose infiltration is relatively common, occurring in 11%–21% of patients according to the current literature (*7,8*); however, the injection site is often out of the FOV. The accuracy of the calculated dose is critical to SUV calculations. Infiltration causes the delivered ^{18}F-FDG dose to be less than the distributed dose. Infiltration on a baseline scan can lead to errors in both the initial and the subsequent treatment strategies. Infiltration may, in fact, contribute to the wide variability in a clinician's success in characterizing SUV thresholds for clinical decision making (*4*). Velasquez et al. found that the "thresholds for metabolic response in the multicenter multiobserver non-[quality assurance] settings were −34% and 52% and in the range of −26% to 39% with centralized [quality assurance]" (*9*). Issues with SUV calculations have left oncologists and researchers needing to see significant changes in SUVs to be somewhat assured they are making sound treatment decisions or reaching proper research conclusions.

The initial stage of our study demonstrated the prevalence of some form of dose infiltration at our facility—a prevalence that was significantly higher than has been reported in the literature. The physicians who evaluated the images identified a rate of 38% (9 minor, 5 moderate, 1 significant) but believed the low threshold for any evidence of uptake at the injection site resulted in this high rate. The physicians noted that none of the 9 minor infiltrations were likely to be clinically relevant. The sensors identified a 55% rate of infiltration (16 minor, 5 moderate, and 1 significant). The disparity between the physicians and the sensors was attributed to infiltrations that had cleared by the time imaging occurred or to injection sites being out of the standard field of view. In such cases, the infiltration may not be visible to the physicians but may still be detectable by the sensors. Additionally, the sensors classified several of the infiltrations differently from the physicians.

The infiltration rate at our institution was initially higher than reported in the literature, possibly because of the additional scrutiny the technologists were under. The technologists suggested that initially they may have felt more pressure while doing the injections, knowing they were being evaluated. Each injection was followed by feedback on its quality. This was the first time the technologists had ever received detailed feedback on their injections, as they could review the time–activity curves immediately after uploading. With each injection, the software gathered information about each technologist's technique. While completing the initial 40 subjects, the technologists began, subconsciously or consciously, to modify and improve their technique. However, the software analysis found only one real association with the technologists' issues. Approximately 92% of their left-side nonantecubital injections infiltrated. Once the data were analyzed and discussed with the technologists, various practice modifications were implemented to reduce the infiltration rate. Many of the modifications were simple changes in technique, such as slowing down and focusing on the injection regardless of what was occurring at the facility. Technologists also switched from a butterfly intravenous line to an Angiocath (Becton Dickinson and Co.) intravenous line, as well as modifying their approach when injecting subjects on the left side (since both technologists were right-handed). Their actions, combined with awareness provided by the software of the need to modify left-side injections, resulted in lower infiltration rates as detected by both the physicians and the sensors. The physician rate went from 38% to 25% (13 minor, 3 moderate, and 1 significant), a reduction of 34%. The sensor rate went from 55% to 6% (2 minor and 2 moderate), a reduction of 89%. The disparity in the physician and sensor results again primarily concerned the number of minor infiltrations. However, in 12 cases of minor infiltration as

TABLE 1
Results for Each of the Initial 40 Patients

Patient no.	Physician reporting		Sensor reporting	
	Infiltration present?	Would SUV be affected?	Infiltration present?	Additional characterization?
1	No		Yes, minor	Yes
2	No		No	No
3	Site not in FOV		Yes, moderate	Yes
4	No		No	No
5	Yes, minor	Not likely	Yes, minor	No
6	No		Yes, minor	Yes
7	Yes, minor	Not likely	Yes, moderate	Yes
8	No		No	No
9	Site not in FOV		Yes, minor	Yes
10	Yes, moderate	Not likely	Yes, moderate	No
11	No		No	No
12	Site not in FOV		No	Yes
13	Yes, moderate	Not likely	Yes, minor	Yes
14	Yes, minor	Not likely	Yes, minor	No
15	Yes, significant	Very likely	Yes, significant	No
16	No		No	No
17	Yes, moderate	Not likely	Yes, moderate	No
18	Site not in FOV		No	Yes
19	Yes, moderate	Possibly likely	Yes, moderate	No
20	Yes, minor	Not likely	Yes, minor	No
21	Yes, minor	Not likely	Yes, minor	No
22	No		No	No
23	No		No	No
24	No		No	No
25	No		No	No
26*	No		Yes, minor	Yes
27	Yes, moderate	Not likely	Yes, minor	Yes
28	No		Yes, minor	Yes
29	No		No	No
30	No		No	No
31	Yes	Not likely	Yes, minor	No
32	No		No	No
33	Yes, minor	Not likely	Yes, minor	No
34	Yes, minor	Not likely	Yes, minor	No
35	Yes, minor	Not likely	Yes, minor	No
36	No		No	No
37	No		No	No
38	No		No	No
39	Yes, minor		Yes, minor	Yes
40	No		No	No

*Injection was in right forearm and within FOV; no injection problems were evident.
FOV = field of view.

classified by the physicians, there was just faint evidence at the injection site. In these same cases, the sensors showed no infiltration.

In addition to the decreased rate of infiltration, the severity of infiltration decreased. Using the time–activity curves as a more complete way to analyze the severity of infiltration over the uptake period, the sensors showed 6 moderate or significant infiltrations in the first 40 subjects (15%). In the next 69 subjects, the sensors showed 2 moderate infiltrations (3%). Although our study showed infiltration to be common, the sensor device allows PET/CT facilities to assess the quality of injections, pinpoint areas for improvement, and cater to each technologist's strengths and weaknesses.

Our study was not without limitations. The study design did not lend itself to a randomized controlled trial since the sensor was used on all subjects. In addition, our technologists were not masked. They received real-time information on their injection outcomes, which influenced the quality improvement process. Conducting a more rigorous quality improvement process at multiple sites may provide more information about the capabilities of the device. Finally, the clinical significance of the infiltrations has yet to be determined.

CONCLUSION

Sensor time–activity curves provided valuable information for identifying infiltration even when the injection site

TABLE 2
Results Classified by Infiltration Extent Before Modifications Were Made

Infiltration extent	Physician reporting	Sensor reporting	Reconciliation
Minor	9	16	Sensor and physician reporting agreed on 8 minor infiltrations, but sensor classified 1 additional as out of the FOV; sensor found mild infiltration in 5 cases where physician found no infiltration and in 2 cases where physician found moderate infiltration
Moderate	5	5	Sensor and physician reporting agreed on 3 moderate infiltrations; sensor found moderate infiltration in 1 case where physician found the injection site to be out of the FOV and in 1 case where physician found minor infiltration
Significant	1	1	Sensor and physician reporting agreed on 1 significant infiltration
Infiltration rate	38%	55%	

FOV = field of view.

TABLE 3
Results Classified by Infiltration Extent After Modifications Were Made

Infiltration extent	Physician reporting	Sensor reporting	Reconciliation
Minor	13	2	Of 13 infiltrations classified as minor on physician reporting, 12 were so minor that sensor did not count them, and sensor agreed that 1 was minor; 1 infiltration classified as moderate on physician reporting was classified as minor on sensor reporting
Moderate	3	2	Of 3 infiltrations classified as moderate on physician reporting, sensor reporting agreed with two
Significant	1	0	
Infiltration rate	25%	6%	

was outside the field of view. Time–activity curves also better characterize infiltration when injection sites are in the field of view, since static images do not always accurately reflect the severity of infiltration during the uptake period. Because inaccurate dose information and the duration of the uptake period are known to affect image quality and SUV quantification, incorporating the device into the injection process in all cases provides valuable quality assurance information to the reading and treating physicians. Additionally, analyzing factors contributing to infiltration adds quality assurance to the center's routine injection process. Our results suggest that the injection process can be improved on the basis of information obtained from the Lara device.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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