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Novel Method to Detect and Characterize F-18 FDG Infiltrations in PET Injections: A Single Institution Experience

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ABSTRACT

Purpose:
A novel Quality Assurance/Quality Control (QA/QC) device provides Time Activity Curves (TACs) which can identify and characterize PET/CT radiotracer infiltrations during the uptake phase. The purpose of this study was to compare rates of infiltration detected by the device compared to standard PET image infiltration rates. We also aimed to assess the value of using the device to improve injection results in our center.

Methods:
109 subjects were consented to the study. All subjects 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 presence of dose infiltration. Sensor-generated TACs were independently examined and then compared to physician reports. Injection process data captured by the software were analyzed; results were provided to technologists. Improvement measures were implemented and rates were re-measured.

Results:
Initial physician review of 40 head-to-toe Field of View (FOV) images identified 15/40 (38%) cases of dose infiltration; 9 minor, 5 moderate, and 1 significant. Sensor TACs on these 40 cases independently identified 22/40 (55%) cases with dose infiltration; 16 minor, 5 moderate, and 1 significant. After TAC results and the contributing factors analysis were shared with technologists, injection techniques were modified and an additional 69 cases were performed. Of these, physician review identified 17/69 (25%) cases of infiltration; 13 minor, 3 moderate, and 1 significant, a 34% decline. Sensor TACs identified 4/69 (6%) cases of infiltration; 2 minor and 2 moderate, an 89% decline.

Conclusion:
The device provides valuable QC information for each subject. TACs provide additional characterization for visible infiltrations. Even when the injection site was out of the FOV, TACs could still detect and characterize these infiltrations. Our initial experience demonstrated the device QA information aided in reducing the infiltration rate and severity. It provided site-specific contributing factors to nuclear medicine physicians and technologists which helped customize quality improvement to the site-specific injection issues. Reducing infiltrations has the potential to improve image quality and SUV quantification as well as the ability to minimize variability in a site's PET/CT results.

INTRODUCTION

With the commercialization of the first PET/CT (positron emission tomography/computed tomography) scanner in 2001, this technology has played an ever-increasing role in oncology, neurology, cardiology, and other various other applications. PET using fluorine-18-2-deoxy-D-glucose (^{18}F-FDG) diagnoses, stages, and restages many cases of cancer. Accuracy ranges from 80% to 90% and is often better than that of anatomic imaging (1-3). Since changes in 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 anatomical imaging is playing an ever-increasing role as a way to quantitatively measure individual response to therapy and to even evaluate new drug therapies (4-5).

The standardized uptake value (SUV) is commonly used as a relative measure of the 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 two largest factors that influence SUV are the injected dose and subject size (5). Primary factors that impact the delivered dose of 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. An infiltration is a common problem that can occur when the radio-labeled 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, infiltrations have the potential to underestimate the metabolic activity of lesions and internal reference points which can affect the interpretation of the study.

While there is very little published information on FDG infiltration rates, they are not insignificant and the impact on SUV is not fully characterized. This study used a novel Quality Control device, Lara, provided by Lucerno Dynamics, LLC (Lucerno; Cary, North Carolina) using Time Activity Curves (TACs) to dynamically characterize the quality of an F-18 injection during the uptake period. The study aimed to compare standard clinical PET images to sensor results for infiltration detection/characterization. When researchers noted initial high infiltration rates, they expanded the scope of the study. Contributing factors were analyzed and shared with technologists, improvements to practice patterns were implemented, and rates were re-measured.

MATERIALS AND METHODS

Patients

The study has been approved by our institutional review board at St 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 exam and asked about interest in participation. 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 and retained by members of the research team.

Sensor application and PET/CT scanning

Once consent was obtained, the subject continued with the standard of care screening process. The Lara devices, consisting of scintillation sensors, pads, reader and docking station, were available in each uptake room. Just prior to the FDG injection, the Lucerno sensors were

placed by the PET/CT technologist on the subject (injection site and contralateral arm; see Figure 1). The device sensors remained in place for the FDG uptake period (typically 60-90 minutes). The subject would sit in a reclined chair for this uptake period. After the uptake time was complete, the sensors were removed by the technologist. The subject then proceeded with True Whole Body PET/CT imaging from head-to-toe, which is the standard of care at our institution for all cancer patients. PET/CT images acquired ~70 minutes post injection. The subject did not receive additional radiation due to the study and the device use only added 1 minute to the time of their PET/CT examination. The study team then uploaded the sensor data and factors collected for each injection to the PC in the PET/CT control room. Some of the factors include, but are not limited to injection location and orientation, needle gauge, injecting technologist, radiotracer, dose, subject height and weight, and subject glucose. Data were then transferred via the internet to Lucerno Dynamics where they were automatically analyzed. After imaging, the subject was asked to complete a brief survey on the comfort of use for the Lara device. This coded paper survey was submitted to Lucerno Dynamics for further development of this device.

Data analysis

Two board certified Nuclear medicine physicians reviewed the standard PET/CT images and assessed for any evidence of uptake at the site of injection. After reviewing images, the Nuclear Medicine physicians completed a report with their findings based upon their experience. TACs generated from the applied sensors were independently examined and then compared to physician reports. TAC information was recorded along with physician report information and differences between the two findings were documented.

After the initial 40 subjects were enrolled, a contributing factor analysis was done and results were shared with the technologists. Improvement measures were implemented and infiltration rates were measured again in the ensuing 69 subjects.

RESULTS

Physician review of static images using head-to-toe FOV for the initial 40 subjects, undergoing standard clinical image uptake processes, found visible evidence of infiltration in 15/40 cases (38%). Sensor TACs on the same 40 cases the physicians reviewed identified infiltration in 22/40 (55%) cases. Of these 40 patients, 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, 2/13 (15%) were injections at the antecubital fossa and 6/7 (86%) were distal to the antecubital. Of the left sided infiltrations, 0/1 (0%) proximal to the antecubital, 3/7 (43%) at the antecubital and 11/12 (92%) distal to the antecubital. Figure 2 depicts TACs obtained from sensor recordings in 3 cases. A detailed review of these results is in Tables 1 and 2.

TAC results and the contributing factors analysis were shared with the technologists injecting the radiotracer. After the implementation of injection technique modifications, physician review of static images using head-to-toe FOV for 69 subjects, undergoing standard clinical image uptake processes, found visible evidence of infiltration in 17/69 cases (25%). Sensor TACs on the same 69 cases the physicians reviewed identified infiltration in 4/69 (6%) cases. A review of these results is in Table 3.

DISCUSSION

The most commonly used injection site for PET/CT exams is the antecubital fossa with other injection sites more distal on the arm. The majority of patients are imaged from the base of the skull to upper thighs with the arms up (6). Studies which have reviewed injection site images have shown dose infiltrations are relatively common, occurring in 11-21% of cases 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 and an infiltration results in the delivered FDG dose being less than the distributed dose. Infiltrations at a baseline scan can lead to errors in initial treatment strategies for the clinician as well as subsequent treatment strategies. Infiltrations may in fact contribute to the wide variability in a clinician's efforts to characterize SUV thresholds for clinical decision making (4). Velasquez found that the "thresholds for metabolic response in the multicenter, multiobserver, non-QA, settings were -34% and 52% and in the range of -26% to 39% with centralized QA" (9). Issues with SUV calculations have left oncologists and researchers needing to see significant changes in SUV values 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 infiltrations at our facility which was significantly higher than has been reported in the literature. The reading physician evaluation of 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 higher rate. Reading physicians noted that all 9 of the minor infiltrations were likely to not be clinically relevant. The sensors identified a rate of 55% (16 minor, 5 moderate, and 1 significant). The disparity between the readers and sensor was attributed to infiltrations which had cleared by the time imaging had occurred and/or to injection sites out of the standard image FOV. In such cases, the infiltrations may not be visible to the readers but could still be detected

by the sensors. Additionally, the sensors classified several of the injections differently than the readers. The infiltration rate at our institution was initially higher than reported in the literature possibly due to the additional scrutiny the technologists were under. They suggested that initially they may have felt more pressure doing the injections knowing they were being evaluated. Each patient came with feedback on the quality of the injection. It was the first time the technologists had ever received detailed feedback on their injections as TACS were visible to them immediately after uploading. Throughout these injections, the software gathered information about each technologist's technique. While performing the initial 40 patients, technologists began to subconsciously or consciously modify their technique to improve. However, the software analysis found only one real association for their issues. Approximately 92% of their left side non-antecubital injections infiltrated. Once the data was analyzed and discussed with the technologists, various practice modifications were implemented in hopes to improve the infiltration rates. 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 IV to an Angiocath IV as well as modifying their approach when injecting patients on the left side (since both technologists were right handed). The combination of their actions along with the awareness provided by the software that they were infiltrating at a high rate on the left side outside the antecubital resulted in improved infiltration rates by both the reading physicians and the sensors. The reader rate decreased from 38% to 25% (13 minor 3 moderate, and 1 significant), a reduction of 34%. The sensor rate decreased from 55% to 6% (2 minor and 2 moderate), a reduction of 89%. The disparity in the reader and sensor results were again primarily in the number of minor infiltrations. However, in 12 minor infiltration cases classified by the readers, there was just faint evidence at the injection

site. In these same cases, the TACs during the uptake period did not result in a minor classification by the sensor. In addition to the overall decrease in the infiltration rate, the severity of infiltrations also decreased. Using the TACs as a more complete way to analyze the severity of infiltrations over the entire uptake period, there were 6 moderate or significant infiltrations in the first 40 patients (15%). In the next 69 patients, there were 2 moderate infiltrations (3%). The results from this study suggest dose infiltrations are a common occurrence but with this device, PET/CT facilities have the ability to assess the quality of injections and pinpoint areas of improvement and cater to each technologist's strengths and weaknesses.

Our study is not without limitations. The study design did not lend itself to a randomized controlled trial since all patients enrolled in the study utilized the sensors. In addition, our technologists were not blinded. They received real-time information on their injection outcomes which impacted the quality improvement process. Conducting a more rigorous quality improvement process at multiple sites may provide more information about the capabilities of the device. Lastly, the clinical significance of the infiltrations has yet to be determined.

CONCLUSION

Sensor TACs provided valuable information to identifying infiltrations even when the injection sites were outside the imaging FOV. TACs also help improve characterization of infiltrations when injections sites are in the FOV, since static images do not always reflect the severity of infiltration during the uptake period accurately. Because inaccurate dose information and the duration of the uptake period are known factors that can impact image quality and SUV quantification, incorporating the device into the injection process provides valuable quality control information to reading and treating physicians in all cases.

Additionally, analyzing infiltrations and injection process contributing factors adds quality assurance to the center's routine injection process. Results from the experience at this center are suggestive of an improved injection process based on information obtained from the Lara device.

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FIGURES AND TABLES

Figure 1. Lara device sensors placed on the injection arm and the contralateral control arm (top). The Lara device consists of 2 scintillation sensors, 2 pads, reader and docking station (bottom).

Figure 2. TACs from sensor recordings in 3 cases. **TOP:** Example of an ideal injection in the right antecubital fossa (red arrow). Injection sensor results (black line) drop immediately (blue arrow) to the reference arm level (red line). **MIDDLE:** Example of moderate infiltration in the left wrist (red arrow). Injection sensor results do not drop immediately (blue arrow) to reference arm level. **BOTTOM:** Example of severe infiltration with the injection in the right antecubital fossa (red arrow). Injection sensor results never fall to the reference arm level.

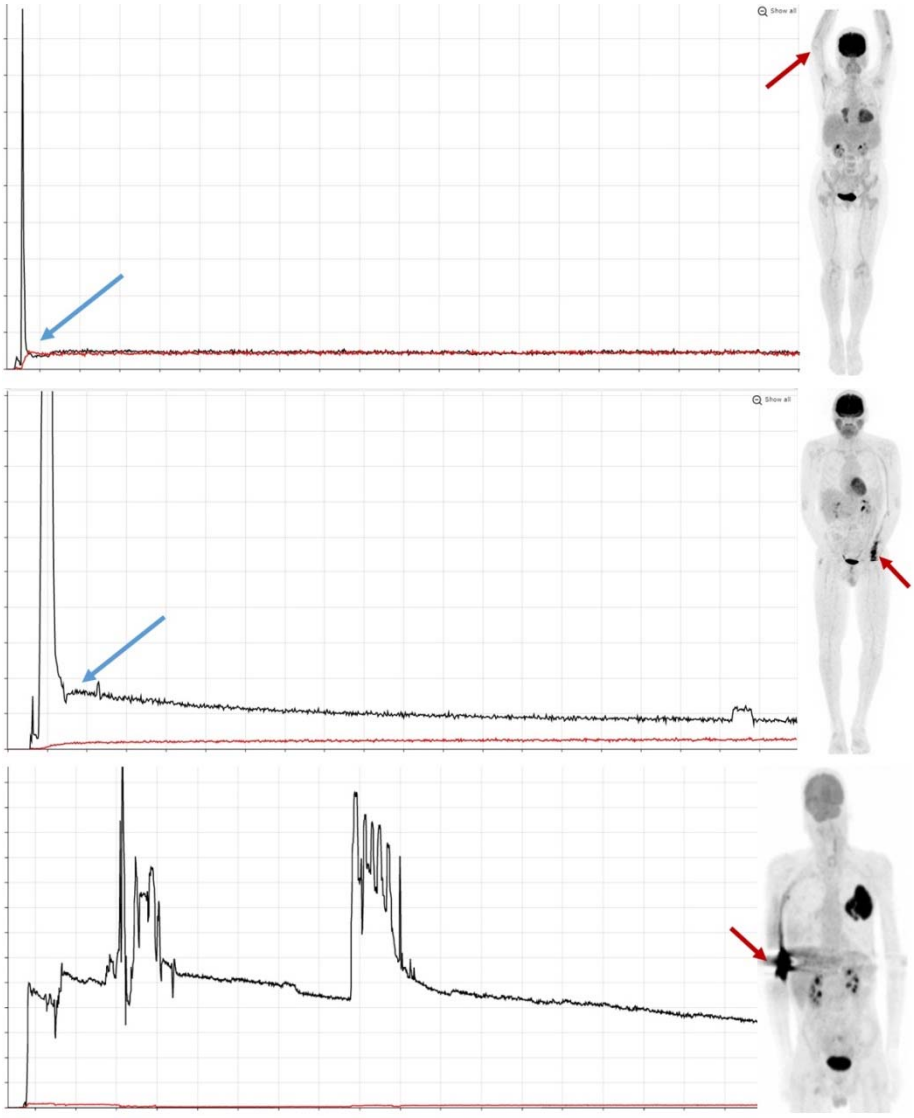

Table 1. Patient characteristics in the initial 40 subjects

Number	Standard Reporting Using Routine Static Image			Lara Reporting		Observations	Additional Characterization and Notes
	Physician Report of Radiotracer at Injection Site	Characterization of Radiotracer if Applicable	Physician opinion on whether or not the infiltration would impact the SUV	TAC Identification of Presence of Radiotracer	Characterization		
1	No	N/A		Yes	Minor Infiltration	Additional characterization	Stasis
2	No	N/A		No	Ideal	Same as Report	
3	Site not in FOV	N/A		Yes	Moderate Infiltration	Additional Characterization	Site not in FOV. Lara TAC identified moderate infiltration.
4	No	N/A		No	Ideal	Same as Report	
5	Yes	Minor Infiltration	Not Likely	Yes	Minor Infiltration	Same as Report	
6	No	N/A		Yes	Minor Infiltration	Additional characterization	Stasis
7	Yes	Minor Infiltration	Not Likely	Yes	Moderate Infiltration	Additional Characterization	Lara TAC indicates more severe infiltration.
8	No	N/A		No	Ideal	Same as Report	
9	Site not in FOV	N/A		Yes	Minor Infiltration	Additional Characterization	Site not in FOV. Lara TAC identified minor infiltration.
10	Yes	Moderate Infiltration	Not Likely	Yes	Moderate Infiltration	Same as Report	
11	No	N/A		No	Ideal	Same as Report	
12	Site not in FOV	N/A		No	Ideal	Same as Report	Site not in FOV.
13	Yes	Moderate Infiltration	Not Likely	Yes	Minor Infiltration	Additional characterization	Lara TAC indicates less severe infiltration.
14	Yes	Minor Infiltration	Not Likely	Yes	Minor Infiltration	Same as Report	
15	Yes	Significant Infiltration	Very Likely	Yes	Significant Infiltration	Same as Report	
16	No	N/A		No	Ideal	Same as Report	
17	Yes	Moderate Infiltration	Not Likely	Yes	Moderate Infiltration	Same as Report	
18	Site not in FOV	N/A		No	Ideal	Additional characterization	Lara TAC confirms no infiltration.
19	Yes	Moderate Infiltration	Possibly Likely	Yes	Moderate Infiltration	Same as Report	
20	Yes	Minor Infiltration	Not Likely	Yes	Minor Infiltration	Same as Report	
21	Yes	Minor Infiltration	Not Likely	Yes	Minor Infiltration	Same as Report	
22	No	N/A		No	Ideal	Same as Report	
23	No	N/A		No	Ideal	Same as Report	
24	No	N/A		No	Ideal	Same as Report	
25	No	N/A		No	Ideal	Same as Report	
26	No	N/A		Yes	Minor Infiltration	Additional characterization	TAC identifies very minor infiltration. Injection was in right forearm and was in the FOV. No evidence of problems with the injection.

27	Yes	Moderate Infiltration	Not Likely	Yes	Minor Infiltration	Additional Characterization	Lara TACs indicate less severe infiltration.
28	No	N/A		Yes	Minor Infiltration	Additional characterization	Minor stasis.
29	No	N/A		No	Ideal	Same as Report	
30	No	N/A		No	Ideal	Same as Report	
31	Yes	Minor Infiltration	Not Likely	Yes	Minor Infiltration	Same as Report	
32	No	N/A		No	Ideal	Same as Report	
33	Yes	Minor Infiltration	Not Likely	Yes	Minor Infiltration	Same as Report	
34	Yes	Minor Infiltration	Not Likely	Yes	Minor Infiltration	Same as Report	
35	Yes	Minor Infiltration	Not Likely	Yes	Minor Infiltration	Same as Report	
36	No	N/A		No	Ideal	Same as Report	
37	No	N/A		No	Ideal	Same as Report	
38	No	N/A		No	Ideal	Same as Report	
39	No	N/A		Yes	Minor Infiltration	Additional characterization	Very minor stasis.
40	No	N/A		No	Ideal	Same as Report	

Table 2. Results of the initial 40 cases

Infiltration Classification	**Physician report of presence**	**Lara TAC determination of presence**	**Results**
Minor	9	16	Lara and SLU agreed on 8 of SLU classified Minor infiltrations. Lara classified 1 site out of FOV. Lara classified 5 injections as minor that SLU saw no evidence of infiltration. Lara classified 2 SLU Moderate infiltrations as minor for a total of 16
Moderate	5	5	Lara and SLU agreed on 3 of SLU classified Moderate infiltrations. Lara classified I site out of FOV as moderate and classified one SLU Minor as Moderate.
Significant	1	1	Both Lara and SLU agreed on one Significant Infiltration
Infiltration Rate	38%	55%	

Table 3. Results of the additional 69 cases after modifications made

Infiltration Classification	**Physician report of presence**	**Lara TAC determination of presence**	**Results**
Minor	13	2	Out of 13 SLU classified minor infiltrations, 12 were so minor that Lara did not count them. 1 of them we agreed was minor. 1 of SLU classified moderate infiltrations Lara indicated as minor.
Moderate	3	2	Out of 3 SLU classified moderate infiltrations. Lara agreed with 2 of them.
Significant	1	0	
Infiltration Rate	25%	6%	