J of Nuclear Medicine Technology, first published online June 10, 2019 as doi:10.2967/jnmt.119.228098

Quality Improvement Initiatives to Assess and Improve Positron Emission Tomography/Computed Tomography Injection Infiltration Rates in Multiple Centers

Terence Z. Wong, M.D[1, 2]. Thad Benefield, M.S[2]. Shane Masters, M.D., Ph.D.[3], Jackson W. Kiser, M.D.[4], James Crowley, MHA, CNMT[4], Dustin Osborne, Ph.D., DABSNM[5], Osama Mawlawi, Ph.D.[6], James Barnwell, M.D.[7], Pawan Gupta, M.D.[8], Akiva Mintz, M.D., Ph.D.[9], Kelley A. Ryan, B.A., M.C.[10], Steven R. Perrin, M.S.E.E.[10], Ronald K. Lattanze, M.B.A.[10], David W. Townsend, Ph.D.[11]

[1]Duke University, Durham, NC, USA, [2]University of North Carolina, Chapel Hill, NC, USA, [3]Wake Forest Baptist Medical Center, Winston Salem, NC, USA, [4]Carilion Clinic Roanoke, VA, USA, [5]University of Tennessee Graduate School of Medicine Radiology/Molecular Imaging & Translational Research Knoxville, TN, USA, [6]Department of Imaging Physics, The University of Texas, MD Anderson Cancer Center, Houston, TX, USA, [7]Wake Radiology, Raleigh, NC, USA, [8]Division of Nuclear Medicine, Department of Molecular and Medical Pharmacology, David Geffen School of Medicine at UCLA Health Los Angeles, CA, USA, [9]Columbia University Medical Center, New York, NY, USA, [10]Lucerno Dynamics, LLC, Cary, NC, USA, [11]A*STAR-NUS Clinical Imaging Research Centre, Singapore

Short Running Title: PET/CT Injection Quality Improvement

Corresponding Author:

David W. Townsend

A*STAR-NUS Clinical Imaging Research Centre

Singapore

dnrdwt@gmail.com

604-935-9446

First Author:

Terence Z. Wong

Chief, Division of Nuclear Medicine

Duke University Medical Center

terence.wong@duke.edu

919-684-7245

Word Count: 4,899

Funding:

This material is based upon work supported in whole or part by the North Carolina

Biotechnology Center.

Abstract

PET/CT radiotracer infiltrations are not uncommon and often outside imaging fields of view. Infiltrations can negatively impact image quality and quantification, and can adversely affect patient management. Until recently, there has not been a simple way to routinely practice PET radiopharmaceutical administration quality control/quality assurance (QC/QA). Our objectives were to quantify infiltration rates, determine associative factors for infiltrations, and to assess if rates could be reduced and sustained at multiple centers.

Methods

A Design, Measure, Analyze, Improve, Control quality improvement (QI) methodology requiring novel technology was used to try to improve PET/CT injection quality. Teams were educated on the importance of quality injections. Baseline infiltration rates were measured, center-specific associative factors were analyzed, team meetings were held, improvement plans were established and executed, and rates remeasured. To ensure injection quality gains were retained, real-time feedback and ongoing monitoring were used. Sustainability was assessed.

Results

Seven centers and 56 technologists provided data on 5,541 injections. The centers' aggregated baseline infiltration rate was 6.2% (range 2% - 16%). Based on their specific associative factors, four centers developed improvement plans and reduced their aggregated infiltration rate from 8.9% to 4.6% ($p<0.0001$). On-going injection monitoring showed sustainability. Significant center- and technologist-level infiltration rate variation was found ($p < 0.0001$ and $p= 0.0020$).

Conclusion

A QI approach with new technology can help centers measure infiltration rates, determine associative factors, implement interventions, and improve/sustain injection quality. Since PET/CT images help guide patient management, monitoring and improving radiotracer injection quality is important.

Key Words: Quality Improvement; PET/CT; Infiltrations; Extravasations; FDG

Introduction

An estimated three million PET/CT procedures were performed in the US in 2017; over 90% for oncology care and ~10% for assessing myocardial perfusion, neurological function, and other physiologic processes (*1,2*). Complete radiotracer intravenous bolus delivery is important to imaging accuracy and reproducibility (*3*) and thus to patient treatment (*4*). A radiotracer infiltration prevents a bolus delivery of the entire dose. Infiltrations happen when a catheter punctures or erodes the venous wall or when injection pressure damages the wall. This leads to fluid infusion into the soft tissue surrounding the vein. Severity of the effect on image quality and quantification cannot be determined precisely (*4*), but depends on the initial infiltrate amount, the rate at which infiltrate reenters circulation, and residual infiltrate amount that never enters circulation.

Unlike other healthcare injection processes that monitor injection quality (e.g., contrast CT and chemotherapy) (*5-7*), there is no evidence PET/CT injections are routinely monitored. Difficulty in detection may be a factor. PET/CT technologists usually inject small radiotracer volumes that do not cause immediate patient pain and rarely cause visible changes to the skin near the injection site. Furthermore, during PET/CT image interpretation, injection sites are often outside of the imaging field of view (*8*). Detection is further hindered when injection sites are in the imaging field of view, but infiltrations have resolved completely leaving no visible evidence (*9*). There is also little published data on PET/CT radiotracer injection infiltration rates. A literature review identified six studies (2006-2017) from three centers that used routine static images as their method to identify infiltrations. These studies involved 2,804 patients and 425 infiltrations

(15.2%). Rates ranged from 3% - 23% (*8,10-14*) and based on detection difficulties, may have underestimated true infiltration rates (*9*).

Our hypotheses were that a quality improvement (QI) approach could: measure infiltration rates for patients undergoing PET/CT exams across multiple centers; determine associative factors that may contribute to infiltrations; and measure the reduction of rates in infiltrations.

Materials and Methods

An Institutional Review Board for each center determined that the project did not meet the definition of research as defined by the federal government in 45 CFR 46.102(d) and therefore, no patient consent was required. No protected health information (PHI) was collected.

Since QI approaches have led to high-quality chemotherapy and contrast CT injection results (*6,7*) in patient populations like those experiencing PET/CT radiotracer injections, following a QI process for PET/CT could lead to similar results. Define, Measure, Analyze, Improve, Control (DMAIC) QI methodology was employed.

In the *Define Phase*, the infiltration problem, injection process, clinician/center needs, and potential factors associated with infiltration were defined in a protocol approved by each center. Seven centers participated on the condition of anonymity and the aggregation of data. Centers were sequentially initiated from December 2016 to July 2017 (approximately one center/month).

Centers included two low-volume (<2 patients/day) outpatient/mobile units, a medium-volume (~5 patients/day) community care hospital, three high-volume (~18 patients/day) academic centers, and a very high-volume (>30 patients/day) cancer care center. Before center initiation, fifty-six certified nuclear medicine technologists (experience ranging from 1-41 years, mean 13.8 years, median 12.5 years), five nuclear medicine physicians, and two physicists participated and were educated on project and injection process importance.

Because nuclear medicine injection quality is not routinely measured, an infiltration detection method was needed to consistently determine baseline performance across centers. Therefore, novel technology was required in the *Measure Phase*. A commercially available system, Lara® (Lucerno Dynamics, Cary, NC) was selected based on clinical studies demonstrating the system's ability to identify presence of radiotracer near the injection site and to help reduce infiltration rates (*9,13,15*). Lara® (the system) includes topical sensors and a reader to collect and store data, software to transfer data, and a web application to display and analyze data. System use adds ~30 seconds to the patient experience and 90 seconds to the technologist experience. The system assists clinicians in assessing injection quality by providing injection and reference arm time-activity curves (TACs) during the uptake period (Figure 1). TACs are scored by an automated classifier, developed from nuclear medicine physician qualitatively-evaluated injections.

Figure 1

In the *Measure Phase*, technologists used the system to monitor radiotracer injections for adult and pediatric patients for a period of 2-4 months, based on center volume. After gaining venous access, and prior to injecting patients with a radiotracer, technologists applied atraumatic adhesive pads and then sensors to the patient. One pad/sensor was applied approximately 7 cm proximal to the injection site, the other was applied in the mirrored location on the contralateral arm. Data were recorded by the system during the tracer uptake period (typically 45 – 60 minutes). Following pads/sensors removal from the patient, technologists uploaded patient- (height, weight, BMI, glucose, age group <16, 16-49, 50-69, >70) and procedure-specific (injecting technologist, venous access method, radiotracer dose, flush volume, needle gauge, injection site location and orientation – right or left) variables to the system's web application. TACs were immediately generated. During this phase, TACs were not available to technologists so that the review did not influence technologist technique. TACs were independently assessed by the system developer. Scores >200 were considered indicative of injection site radiotracer presence. Scores >1,000 were communicated to center PIs to ensure interpreting physicians were aware of potential patient care implications, caused by radiotracer presence near the injection site. Re-imaging and assessing the potential clinical effect of radiotracer presence were outside the project's scope. Weekly utilization data (number of TACs compared to number of PET/CT patients) were collected, analyzed, and reported to centers to encourage system use. After this phase and throughout the remainder of the project, technologists received TAC injection feedback immediately after uploading data.

The *Analyze Phase* began with group-level team meetings at each center. Utilization rates and TACs were reviewed and discussed by the team. Center PIs confirmed measured infiltration rates. The system provided center-specific insight into potential factors associated with poor quality injections by analyzing patient- and procedure-specific variables collected from *Measure Phase* injections.

Four centers proceeded to the *Improve Phase*; each held brainstorming sessions and created specific improvement plans based on associative factors and injection improvement interventions/ideas (Supplemental Table 1). After improvement plans were implemented and injection practices modified, centers remeasured rates by monitoring a similar number of injections by the same *Measure Phase* technologists. At the end of the *Improve Phase*, utilization rates, TACs, infiltration rates, and adherence to improvement plans were evaluated.

After completing their *Improve Phase*, three centers monitored injections for an extended period of time to assess sustainability of injection quality improvement in the *Control Phase*, while the fourth center completed their *Improve Phase*. Ongoing group and individual level feedback were provided real-time during this phase. Documenting qualitative performance feedback for each technologist was outside the project's scope. Overall project data collection ceased for all centers when the fourth center completed their *Improve Phase*. After project completion, all four centers continued to monitor injection quality to ensure routine QC/QA.

Statistical Methods

Co-Primary Endpoints

The first co-primary endpoint was the aggregated infiltration rate across *Measure Phase* centers. Unadjusted rates were calculated by dividing the total number of infiltrations (for all centers) by the total number of injections. Adjusted rates were calculated using a multilevel generalized mixed model, accounting for technologist-, center-, and patient-level correlations. The second co-primary endpoint was the aggregated adjusted rate of reduction in infiltration rates (aggregated *Measure Phase* rate minus their aggregated *Improve Phase* rate) across the *Improve Phase* centers. The p-value for the test of H_0: *no difference between the Improve and Measure Phase adjusted infiltration rates* was reported.

Secondary Endpoints

There were four secondary endpoints:

1. identify associative factors most likely to lead to infiltration,
2. evaluate each *Improve Phase* center's infiltration rate reduction,
3. assess each center's improvement plan adherence, and
4. evaluate variation in infiltration rates at the technologist or center level.

To identify associative factors most likely to lead to infiltration, aggregated data gathered during the *Measure, Improve, and Control Phases* were used to assess associations with injection quality. Main effects (patient- and procedure-specific variables) along with possible two-way interactions were evaluated (see Supplemental Table 2 for details).

To evaluate the rate of reduction of infiltration, centers needed to complete the *Analyze and Improve Phases*. Binary decisions trees and logistic regression were used to assess candidate covariates associations with injection quality during the *Analyze Phase* (see Supplemental Table 3 for details). The percent infiltration rates reduction for *Improve Phase* centers was defined as 100 x [(*Improve Phase* rate - *Measure Phase* rate)/*Measure Phase* rate].

To estimate each center's improvement plan adherence, interventions were categorized as a one-time or ongoing activity. Based on intervention adherence and its ability to affect injection quality, a centers qualitative overall adherence to a proposed improvement plan was estimated (Supplemental Table 1).

To evaluate variation in infiltration rates at the center or technologist level, a likelihood ratio test using the pseudolikelihood was conducted on data from all phases and centers.

Exploratory Analysis

To assess improvement plan sustainability, differences were tested between the *Control* and *Measure Phase* infiltration rates, and between the *Control* and *Improve Phase* rates. P-values were adjusted using Tukey's method to control for Type 1 error.

Results

Data were collected on 5,541 injections: 2,429 *Measure Phase* injections, 1,349 *Improve Phase* injections, and 1,763 *Control Phase* injections. *Measure Phase* device utilization ranged from

30%-99% (mean and median utilization 91% and 93%, respectively). *Improve Phase* utilization ranged from 85-93% (mean and median utilization 90% and 91%, respectively). Technologist infiltration rates ranged from 0%-24.4%.

Co-Primary Endpoints

The aggregated unadjusted infiltration rate for the seven *Measure Phase* centers, was 6.2% (range 1.9% to 15.7%) (Table 1). The aggregated adjusted infiltration rate was 5.7% (SE: 1.8%, 95% CI: [3.0%, 10.6%])

Table 1.

Measure Phase injections characterizations are summarized in Supplemental Table 4.

For the four *Improve Phase* centers*,* the aggregated adjusted *Measure Phase* infiltration rate was 8.9% (SE: 3.4%, 95% CI: [4.2%, 18.2%]). The aggregated adjusted *Improve Phase* rate was 4.6% (SE: 1.9%, 95% CI: [2.1%, 10.0%]) (Table 2). The difference in rates between *Improve and Measure Phases* was 4.3 percentage points, a 48% reduction. The test of H_0: *Measure Phase and Improve Phase rates are equal* yielded a p-value <0.0001, indicating the overall *Improve Phase* infiltration rate was significantly lower than the overall *Measure Phase* rate.

Table 2.

Secondary Endpoints

The all phases' factors most likely to be associated with infiltration were: non-antecubital fossa injection locations, radiotracer dose, flush volume, and patient weight (Table 3). The rate of reduction at *Improve Phase* centers ranged between 10.0% and 78.4% (median 46.6%) (Table 2). Improvement plan adherence was: center A – high, center B – moderate/low, center C – moderate, center D – low. A detailed adherence review is found in Supplemental Table 1. Using data from all phases, the variation in infiltration rates at the center or technologist level was significant. ($p < 0.0001$ and $p= 0.0020$, respectively).

Table 3.

Exploratory Result

Three centers completed a *Control Phase* for an average of 22 weeks (range 15.4 to 25.8 weeks) to assess sustainability of results. This phase was nearly twice the duration and monitored approximately twice as many injections as their *Measure* and *Improve Phases*. All centers improved unadjusted infiltration rates, as compared to the *Measure* and *Improve Phases*. The aggregated *Control Phase* adjusted infiltration rate was 5.2% (Table 4). The test of H_0: *Measure Phase and Control Phase rates are equal* yielded a Tukey-adjusted p-value <0.0001 indicating that the *Control Phase* infiltration rate was significantly lower than the *Measure Phase* rate. The test of H_0: *Improve Phase and Control Phase rates are equal* yielded a Tukey-adjusted p-value=0.55, indicating the *Control Phase* was not significantly different from the *Improve Phase*.

Table 4.

Discussion

PET/CT is a sensitive imaging modality with respect to cancer (*16,17*). Oncologists use PET/CT images to help diagnose and stage disease, choose therapy and plan treatments, and assess tumor response or longitudinally monitor patients (*1,18*). PET/CT is also used in other clinical applications. Injection infiltrations can reduce the sensitivity of PET/CT (*19*), understate SUV values (*4,8,13,15,20,21*) and may cause other imaging issues. An initial literature review of PET/CT injections for oncology and other clinical applications found that infiltrations have or can negatively affect patient management (Supplemental Table 5).

In healthcare settings where infiltrations cause acute patient harm, injections are routinely monitored, infiltrations are detected and reported, and injection results are assessed by accreditation organizations. In these settings, QI efforts have caused infiltration rates to decline to very low levels; yet, clinicians continue to make large-scale efforts to drive rates even lower. Chemotherapy infiltration rates in the 1980s/1990s ranged from 3-6% (*5*). A recent infiltration benchmarking attempt assessed 739,832 patients and reported a 0.1% chemotherapy infiltration rate (peripheral IV and central venous access device infiltration rates were estimated at 0.18% and 0.01% respectively) (*6*). A 1991-2007 review of CT nonionic iodinated contrast medium infiltration studies revealed an average rate of 0.45% (*22*). In 2015, A National Data Registry and Practice Quality Improvement Initiative involving 454,497 CT scans showed rates had improved to 0.24% (*7*).

Our literature review found no such large-scale nuclear medicine injection improvement efforts. Our project confirmed that by using new technology, centers could routinely monitor injections, establish baseline infiltration rates, and determine center-specific factors (Supplemental Figure 1) that enable QI processes to reduce PET/CT injection infiltration rates.

The QI project design had its strengths and limitations. The multi-center approach monitored 5,541 injections, nearly double the previously published number of monitored injections. The project demonstrated injection quality improvement across diverse provider types with different practices, patient volumes, and technologists of varying experience. The project's prospective nature was also a strength, leading to improved injection processes by employing standardized methods to establish infiltration rates, collecting factors associated with injections, and providing individual injection QC.

The project had limitations. Device use added 30 seconds to the PET/CT procedure for patients and added 90 seconds/patient to technologist's workloads (sensor application/removal and providing injection/patient variables). Center representation was a limitation. Five centers supported either academic or NCI-designated comprehensive cancer programs, which comprise 18% of US cancer programs but represented 94.5% of the project's *Measure Phase* injections (Supplemental Table 6). The other two centers supported community providers, and no Veterans Administration centers joined the project. Not collecting injection volume, a potential factor associated with infiltrations, was also a

limitation. Radiotracer injection volume data should be captured in future radiotracer QI projects to further examine the dose and infiltration rate association. Three centers did not move beyond their *Measure Phases*. Their decisions were not contingent on *Measure Phase* results. One center was replacing PET/CT scanners, but remains interested in the *Analyze and Improve Phases*. One radiology group transitioned providers. The third cited time constraints that prevented moving on. While the overall injection utilization rate was high, lack of 100% utilization is also a project limitation. Finally, the trial/observer effect was evident throughout the project. Technologists were reminded of the importance of high-quality radiotracer injections; as a result, it is possible that this trial/observer effect contributed to higher quality project injections.

The combination of trial/observer effect, less than 100% utilization, and the overrepresentation of academic centers and cancer programs suggest the reported *Measure Phase* rates are likely less than the actual incidence of PET/CT injection infiltrations in the US. The lack of 100% utilization likely biased the tests of *Improve and Measure Phase* differences towards the null;100% utilization would likely have resulted in more pronounced differences.

The project has implications for practice and studies in the field. In the current clinical setting, QC measures require that an accurate dose is *administered* to patients (*23*). Based on our findings and published infiltration rates it is important to add a QC measure that ensures the entire dose *enters circulation*. Not all infiltrations will make a difference to patient care, but some will. Just as patient glucose level, syringe residual, and the time of imaging post-injection

are monitored and reported today, providing injection process QC and including this information in PET/CT reports may prove useful. In addition, since the system can be used for different radiotracer energy levels, a QI methodology could be used to improve some of the 15.5 million annual gamma camera scan injections in the US (*1*). Many characteristics associated with PET/CT injections (technologists, patients, technique, and lack of feedback) also exist in gamma camera dose injections. Infiltrated gamma camera procedure injections can also negatively affect patients (*24*).

Preventing infiltrated injections will become even more important as nuclear medicine procedures grow in the future (*1,2,25*). As efforts are implemented to lower radiotracer doses as low as reasonably achievable (ALARA), the infiltrate volume will represent a higher proportion of the administered dose. Finally, the growing use of alpha and beta emitting therapeutics is notable. Where infiltrations of diagnostic radiotracer can result in indirect negative effects for patients, infiltrations of therapeutic radiopharmaceuticals may cause acute and severe patient harm (*26*).

Large radiotracer injection studies, similar in scale to chemotherapy and contrast CT injection studies, are needed to provide insight into the frequency and consequences of nuclear medicine infiltrations. They may identify factors clearly associated with infiltrations and lead to guideline standards that improve injection quality. Nuclear medicine technologist schools could adopt these findings to train future technologists. Additionally, studies into the effect that infiltrations have on image quantification could provide tools that help clinicians provide guidance to reschedule or proceed with imaging infiltrated patients.

Conclusion

To realize the full diagnostic potential of radiotracer imaging, it is important to perform PET/CT and gamma camera scanning with the highest image quality. Minimizing low-quality radiotracer injections could improve nuclear medicine accuracy and reproducibility. This project demonstrated that nuclear medicine infiltration rates can be reduced and sustained through QI. Ongoing monitoring of nuclear medicine injection processes will help ensure that injection processes remain in control or continue to improve, just as contrast CT and chemotherapy injection process have continued to improve. Certified Nuclear Medicine Technologist training programs and accrediting organizations could consider adopting injection monitoring as part of their efforts to improve quality and repeatability of PET/CT and other nuclear medicine scans.

Disclosures

SM, OM, JB, PG, AM – no conflicts

SP, KR, RL - Lucerno Dynamics employees

TB - employee of UNC Chapel Hill, which received statistical support funding

DO - non-financial support from Lucerno Dynamics and is engaging in ongoing research discussions and collaborations outside submitted work

TW, JC, and JK - personal fees from Lucerno Dynamics, outside submitted work

DT - no COI with this project, but holds a PET/CT patent with royalties paid

Devices provided by Lucerno Dynamics free of charge for duration of QI project

Key Points

- QI efforts using novel technology help centers significantly reduce PET/CT injection infiltration rates. On-going monitoring suggests sustainable improvement.

- Injection infiltration rates ranged from 2%-16%, supporting previously published single center rates (3%-23%). Infiltration rates for technologists ranged from 0%-24%.
- The variation in infiltration rates at the center or technologist level was statistically significant.

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Figure Legends

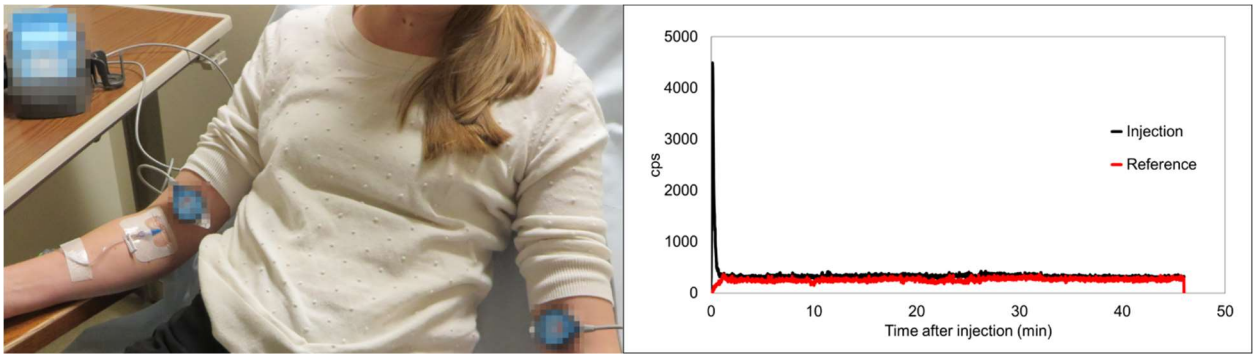


Figure 1. System consists of 2 scintillation sensors, 2 pads, reader and docking station. Sensors placed on injection arm and contralateral arm. Time-activity curve provided after data upload.

Tables

Table 1. Unadjusted *Measure Phase* Infiltration Rates – Note: centers' volumes not included to ensure center anonymity

Center	*Measure Phase* Infiltration Rate
A	13.3%
B	15.7%
C	12.8%
D	2.1%
E	3.2%
F	2.7%
G	1.9%

Table 2. Unadjusted *Measure and Improve Phase* Infiltration Rates – Note: centers' volumes are not included to help ensure individual center anonymity

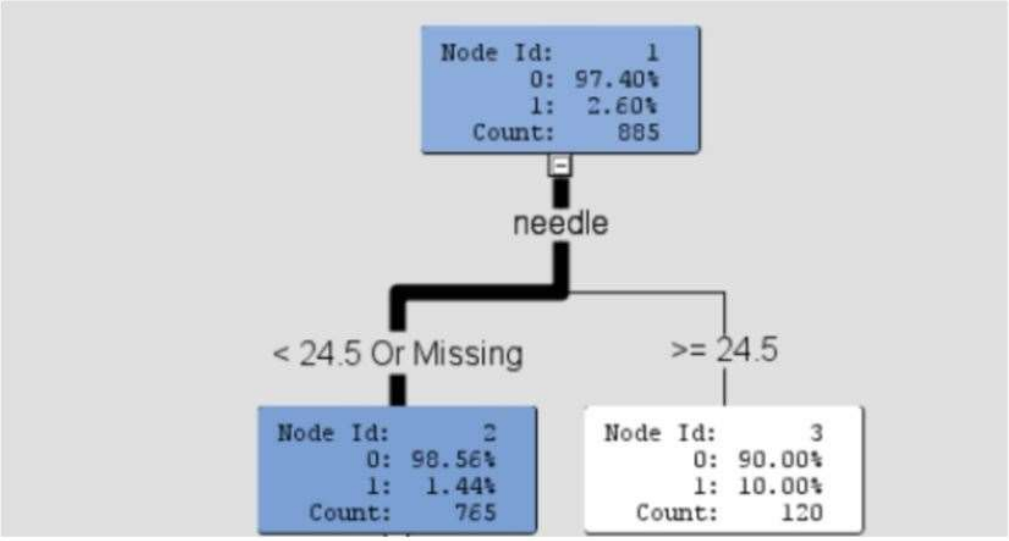
Site	*Measure Phase* Rate	SE	*Improve Phase* Rate	SE	Change
A	13.3%	2.1%	2.9%	1.0%	-78%
B	15.7%	4.0%	6.0%	2.6%	-62%
C	12.8%	1.5%	8.7%	1.3%	-32%
D	2.1%	0.6%	1.9%	0.6%	-10%

Table 3. Associative Factor Analysis for Binary Infiltration Outcome – Significant Associations

Effect (All Data, All Phases)	p Value
Hand/wrist/forearm injections are associated with higher predicted probability of infiltrations when compared to an antecubital fossa injection	$p<0.0001$
Radiotracer dose is positively associated with infiltrations	$p<0.0001$
Weight is negatively associated with infiltrations	$p<0.0001$
Flush volume is negatively associated with infiltrations	$p<0.0001$

Table 4. Sustainability for Three Centers (*Control Phase*) Using Aggregated Rates

Phase	Adjusted Three Center Aggregated Infiltration Rate	Number of Injections	Standard Error	95% CI
Measure	12.1%	815	2.4%	8.2, 17.5
Improve	6.2%	830	1.4%	3.9, 9.5
Control	5.2%	1,763	1.1%	3.5, 7.8



Supplemental Figure 1. Decision tree analysis at one center indicates needle gauge is highly associated with infiltrations. A review of the top box in the figure indicates that 2.6% of the 885 patients were infiltrated. When needle gauge is evaluated for an association, the decision tree indicates that needle gauge >= 24.5 was used for 120 injections and resulted in a 10% infiltration rate (lower right, white box). A needle gauge < 24.5 was used in 765 injections and resulted in a 1.44% infiltration rate (lower left, blue box).

Supplemental Table 1. Adherence to Quality Improvement Plans.

Center	QI Plan Action	Category	Ability to Measure	Estimated Adherence to Measures
A	Addition of auto-injector	Ongoing	H	66%
A	Provide in-service on injection process	One time	H	100%
A	Peer review and sharing of findings	One time	H	100%
A	Evaluate injection room set-up to ensure adequate access on right/left	One time	H	100%
A	**Overall Estimate of Adherence to QIP**			**High**
B	Re-position injection chair for left arm injections	One time	H	100%
B	Switch to IV on left side	Ongoing	H	21%
B	Switch to IV on patients <145lbs	Ongoing	H	14%
B	Switch to IV on patients >70 years	Ongoing	H	50%
B	Standardize/slow the flushing process	Ongoing	M	100%
B	Technologist peer review, sharing of findings, identifying best practices	Ongoing	M	100%
B	Work with patients to minimize movement post-injection to improve quality of image	Ongoing	M	100%
B	**Overall Estimate of Adherence to QIP**			**Moderate/Low**
C	Change injection guidelines in PET protocol	One time	H	100%
C	Use best available vein rather than pre-defined target vein	Ongoing	M	Min
C	Remind patient to be still while tech gets dose ready	Ongoing	L	Good
C	Re-check status of IV after returning to the injection room	Ongoing	L	Good
C	Moderate saline flush rate (at discretion of technologist)	Ongoing	L	Good
C	In-service on injection best practices	One time	H	100%
C	Confirm handedness of all technologists	One time	H	100%
C	**Overall Estimate of Adherence to QIP**			**Moderate**
D	Use blood pressure cuff rather than a tourniquet to improve venous access	Ongoing	H	21%
D	Add a warm compress for several minutes prior to injection for all patients < 135 lbs.	Ongoing	M	19%
D	Contact all patients evening prior to appointment to encourage adequate hydration	Ongoing	L	L
D	Ask 3 questions prior to injection on water consumption	Ongoing	H	Min
D	**Overall Estimate of Adherence to QIP**			**Low**

Supplemental Table 2. Evaluation Methodology of Possible Two-Way Interactions

	Identifying associative factors most likely leading to infiltrations
Step 1	A two-step model selection process was implemented, first using a forward selection procedure with a liberal (p=.1) entry criterion, assuming independence of observations, and second a backward elimination selection procedure after adding in random effects at the center-, technologist-, and patient-level.
Step 2	Where interactions were found to be significant involving binary variables, the least square means was tested for a difference from zero for all covariate combinations.
Step 3	A Bonferroni correction was employed for step 2 to ensure appropriate Type 1 error control.
Step 4	Significant least square means were reported, along with the direction of other significant main effects not part of an interaction

Supplemental Table 3. Assessing Associations with Injection Quality

Approach	Method
Binary decision trees	Binary decision trees were constructed using 20-fold cross validation with inverse prior weights as the assessment measure (SAS Enterprise Miner, v. 14.1).
Logistic regression	Logistic regression using the Bayesian Information Criterion (BIC) as the selection criterion was also employed (SAS v. 9.4). All main effects, along with 2- and 3-way interactions, were evaluated.

Supplemental Table 4. *Measure Phase* Injection Characteristics

	Number of Injections	% of Total
Venous Access Technique		
IV	1881	77.4%
Butterfly	491	20.2%
Indwelling IV	57	2.3%
Needle Gauge		
22	1042	42.9%
24	607	25.0%
23	338	13.9%
20	236	9.7%
25	155	6.4%
14, 19, 21		≤0.1% each
Location		
Antecubital	1721	70.9%
Hand	390	16.1%
Forearm	164	6.8%
Wrist	150	6.2%
Other	4	0.2%
Orientation		
Right side	1484	61.1%
Left Side	945	38.9

Supplemental Table 5. Clinical Impact of Infiltrations

PET/CT Use	Clinical Impact
Oncology Staging	*Under Staging can lead to unnecessary surgery, with the associated morbidity and cost, and it delays the initiation of necessary systemic treatment.* • Missed metastatic disease due to degraded PET/CT image quality, inaccurate quantification results, (*4,20,27*) or significant artifacts in the image. (*27*) • Metastatic disease, identified near an expected injection site location, can be misinterpreted as an infiltration. (*28*)
	Over Staging of a local lesion can lead to treatment for metastatic disease, while withholding potentially lifesaving regional therapy from the patient. • Infiltrations can cause false positive lymph nodes when there is no obvious evidence of an infiltration, (*27-33*) false positive bone scans, (*34*) and spurious lung lesions caused by radioactive clots from injection issues. (*10,27,30,35*)
Oncology Therapy Assessment	• Infiltrations can also lead to therapy assessment errors, due to understated quantification of baseline or follow-up scans. (*8,11,21,36,37*) • An infiltrated baseline study, compared with a properly injected follow-up study, may falsely indicate disease progression. An

	infiltrated follow-up study, compared with a properly injected baseline study, may falsely indicate response to treatment. The previous examples provide specific outcomes that may result from an infiltration, but these injection issues can also cause ambiguous PET/CT results. These can lead to unnecessary invasive procedures or repeat scans, with additional radiation exposure. (*8,20,27-34,36,38*)
Radiation Oncology Planning	• The "definition of the gross tumor volume is the single most important step in the planning process, and all other steps depend upon it. If the tumor is not well imaged and the gross tumor volume is wrong, then the entire treatment process may be futile". (*38*) In quantitative assessment of the gross and clinical tumor volume, an infiltration alters thresholds because of lowered count rates) and therefore provides an incorrect planning treatment volume. (*38*)
Myocardial Perfusion Study	• A rest or stress exam injection infiltration can directly lead to either a false positive or false negative misinterpretation of the study, with serious consequence for patient management. (*4,24,39,40*)
Neurological Function Study	• An infiltration limits the FDG uptake in the brain and can adversely affect the reported results. (*41*)

Amyloid Plaque Study	• Used for Alzheimer's disease and dementia diagnosis, an infiltration can cause poor image quality (due to low counts) and can lead to study misinterpretations. (*42*)
Fever of Unknown Origin Study	• Fever of unknown origin cases have mortality rates range from 12-35% and where more than 50% of these cases cannot be diagnosed using conventional imaging. PET/CT imaging shows relatively high sensitivity and specificity and can be used to improve diagnosis. (*43*) However, an infiltration may compromise imaging sensitivity and diagnostic capability.

Supplemental Table 6. Commission on Cancer (CoC) Classification of Cancer Programs

	Number	Number Grouped	%	Lara QI sites
Academic Comprehensive Cancer Program	188	188	14%	A, D, E
Comprehensive Community Cancer Program	565			
Community Cancer Program	380	945	72%	
Integrated Network Cancer Program	70	70	5%	
NCI Designated Network	6			
NCI Designated Comprehensive Cancer Program	41	47	4%	C, F
Veterans Affairs Cancer Program	36	36	3%	
Freestanding Cancer Center Program	5			
Hospital Associate Cancer Program	10			
Pediatric Cancer Program	10			
Oncology Medical Home	10	35	3%	
Total Programs	1,321	1,321	100%	
Note: Centers B and G were not listed by the CoC as cancer programs				