Background
Radiopharmaceutical extravasation can result in high concentrations of activity remaining within tissue near the injection site resulting in significant cases of radiation exposure as well as unnecessary medical costs. As a result, several techniques have been developed to estimate initial extravasation activity and volume from imaging data. These techniques are characterized by a lack of accuracy in both precision and accuracy. A novel technique was developed to estimate initial extravasation activity from imaging data.

Methods
Estimation of the rate of biological clearance was made using topical injection site sensors (Lara®, Lucerno Dynamics). The sensors provide a measurement every second and the change in their output is a representative of changes in local activity (19). The time-activity curve (TAC) produced by Lara for ideal intravenous injections shows an initial bolus spike from the injection-arm sensor followed by an immediate reduction to a level consistent with that measured by the reference arm sensor. This indicates that the injected radiopharmaceutical is systemic with low probability of residual injection site activity.

An extravasation that leaves significant activity near the injection site results in an elevated TAC data point. In such a situation, sensor output will decrease accordingly. Sensor output and the presence of residual activity at the injection site has been clinically validated using dynamic imaging (20). The figure to the right shows examples of TAC from both ideal and non-ideal injections. With the availability of TAC data for the injection site, one can improve upon the existing extravasation dosimetry techniques.

Overall, the steps in our novel technique are:
1. Calculate the activity clearance rate using injection site TAC data with a least squares fit of an exponential function.
2. Determine the imaging-time extravasation activity and volume using static imaging.
3. Extrapolate backwards to injection time using imaging time activity data and the clearance rate to find initial extravasation activity.
4. Calculate the minimal and maximal initial extravasation volume using injected radiopharmaceutical and saline volumes.
5. Determine the activity within the initial extravasation tissue volumes at imaging time using nuclear medicine data centered on the maximal voxel.
6. Calculate the activity over time within the initial extravasation volumes to determine the potential function to the initial activity.
7. Calculate the dose per unit time for the initial extravasation tissue volumes based on published data for spherical volumes of muscle.
8. Integrate over the physical half-lives to find the total dose to the initial extravasation volumes.

Note: Dose is only calculated for the initial extravasation tissue because this tissue would be exposed to the highest concentration of activity for the longest period of time. This limits assumptions and simplifies calculations, but does result in an underestimation of the true total tissue dose.

Results
Below are the dosimetry results for three clinical cases of diagnostic radiotracer extravasation using the proposed technique.

Conclusions
We have described and demonstrated a novel technique for calculating equivalent dose to tissue in the case of radiopharmaceutical extravasation.

The technique differs from existing techniques by accounting for the ways in which both the extravasation activity and volume change over time. Nuclear medicine practitioners may reject technique 1 as impractical because the assumption of 100% extravasation with no biological clearance is easily refuted by static images. If all activity becomes extravasated, the radiopharmaceutical is considered to be 100% extravasated.

Neither technique 2 nor 3 accurately account for changes over time. Technique 2 assumes biological clearance with a half-time of 120 minutes, whereas the exact half-time is unknown. These procedures use relatively higher injected activity than other procedures, and Tc99m has a significantly longer physical half-life than other radiopharmaceuticals.

Along with the impact that extravasations can have on diagnosis and subsequent treatment (15), there is evidence that the radiation dose to injection site tissue can cause both deterministic (>4.5 Gy) and stochastic (2) harm.

We propose that patient care teams should be aware of and prepared for the possibility of extravasation when using radiopharmaceuticals for diagnostic purposes. Furthermore, they should monitor each procedure for extravasation and assess the radiopharmaceutical extravasation dosimetry. The method demonstrated a novel technique that may be more accurate than existing methods due to inclusion of dynamic time activity data.