Statistical Analysis Plan:

Title of Study: Novel Gallium 68 Citrate Imaging in Orthopedic Infections.
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The purpose of the study is to demonstrate the feasibility and evaluate the accuracy of 68Gallium (^{68}Ga)-citrate positron emission tomography/computed tomography (PET/CT) in diagnosing prosthetic joint infection and compare it with ^{18}fluorine-fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT). We expect that ^{68}Ga-citrate PET/CT will serve as a novel molecular-based sensitive functional imaging modality superior to FDG-PET/CT. We intend to translate the results of this preliminary study to fuel larger studies in the utility of ^{68}Ga-citrate PET/CT to evaluate prosthesis complications, where current available imaging techniques are challenging.

For each subject, we will record the presence and location of abnormal uptake on both 67Gallium Citrate and Fluorodeoxyglucose PET/CT scans. We will then generate a region-of-interest around each area of morphologic abnormality to calculate a mean standardized uptake value (SUV), a maximum SUV, and a target-to-background ratio. These values will be compared with those of contralateral normal joint. Radiotracer uptake pattern on each modality will be classified according to known methods. Using the macroscopic intraoperative and later tissue histology and culture as the gold standard, sensitivity, specificity, and positive and negative predictive values of Ga and FDG PET will be calculated and compared with each other.

For each subject, we will record the presence and location of abnormal uptake. For the PET/CT images, we will generate a region-of-interest (ROI) around each area of morphologic abnormality to calculate a mean standardized uptake value (SUV), a maximum SUV, and a target-to-background ratio. A target-to-background ratio of at least 2.0 will be used to score a particular ROI as positive. These values will be compared quantitatively with those of contralateral normal joint. Radiotracer uptake pattern on each modality will be classified according to known methods. Then, we will descriptively and quantitatively correlate ^{68}Ga-citrate PET/CT findings with those of ^{18}F-FDG PET/CT. Using the macroscopic intraoperative and later tissue histology and culture as the gold standard, sensitivity, specificity, and positive and negative predictive values of Ga and FDG PET will be calculated and compared with each other. We will also review the PET/CT images for multifocal involvement, if any.

Statistical Analysis:

- Primarily, all variables will be analyzed and overall, descriptively, as follows:
- Mean. standard deviation, median and range for continuous variables
- Median, range and frequency distribution for discrete (ordinal) variations

- The results of the imaging modalities (PET, CT and MRI) will be classified as true positive (TP), true negative (TN), false positive (FP), or false negative (FN) according to the reference standard.
- The McNemar test of correlated properties will be used to statistically compare the imaging results of ^{68}Ga-citrate and ^{18}F-FDG PET with MRI and diagnostic CT.
- The student t-test will be used to statistically compare the quantitative findings of ^{68}Ga-citrate and ^{18}F-FDG scans.
- Analysis will be done on a lesion basis and on a patient basis.
- All P values, <0.05 will be considered significant.
- Cohen's k-statistic with 95% confidence intervals will be calculated to show the degree of association between the techniques.