Combined ^{18}F NaF/^{18}F FDG PET/MRI for Detection of Skeletal Metastases

Principal Investigator:

Andrei Iagaru, MD
Co-Chief, Division of Nuclear Medicine and Molecular Imaging
Associate Professor of Radiology - Nuclear Medicine
300 Pasteur Drive, Room H-2230
Stanford, CA 94305
Phone: 650 725 4711
Fax: 650 498 5047
Email: aiagaru@stanford.edu

Co-investigators:

Guido Davidzon, MD
Clinical Assistant Professor, Radiology-Nuclear Medicine

Andreas Loening, MD, PhD
Assistant Professor of Radiology

Shreyas Vasanawala, MD, PhD
Chief of MRI
Associate Professor of Radiology

Biostatistician:
Alex McMillan, PhD

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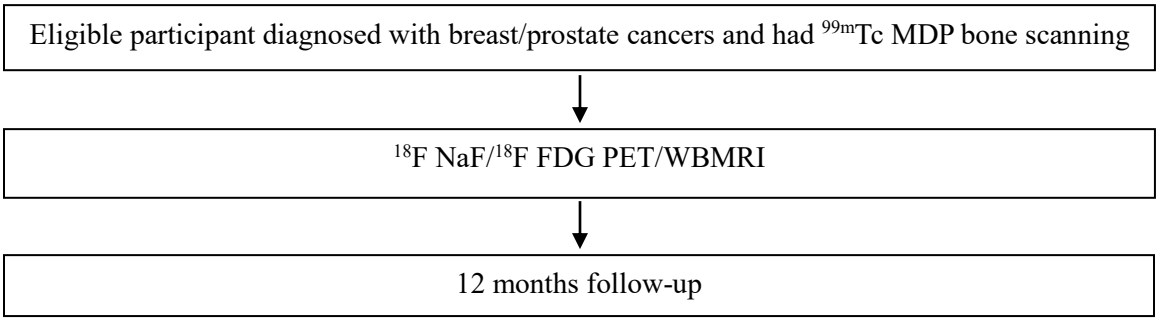
PROTOCOL SYNOPSIS

In the table below summarize the basic aspects of this research. This is to be used as a quick reference guide. Remove any section that is not relevant to the research.

TITLE	Combined ^{18}F NaF/^{18}F FDG PET/MRI for Detection of Skeletal Metastases
INDICATION	Breast cancer, lung cancer, prostate cancer
INVESTIGATIONAL PRODUCT OR PROCEDURE	^{18}F NaF/^{18}F FDG PET/MRI
PRIMARY OBJECTIVE	Testing the hypothesis that the new simultaneous combined ^{18}F NaF/^{18}F FDG PET/MRI provide improved diagnostic accuracy over ^{99m}Tc MDP bone scanning
SECONDARY OBJECTIVE	• Evaluating the combined ^{18}F NaF/^{18}F FDG PET/MRI as a reliable bone scanning modality • Evaluating the performance and reliability of the proposed WBMRI sequences
TREATMENT SUMMARY	No treatment
SAMPLE SIZE	170 participants: 10 from the pilot phase, 30 from PET/CT vs. WBMRI, 80 from first version of combined ^{18}F NaF/^{18}F FDG PET/MRI and 50 from second version of combined ^{18}F NaF/^{18}F FDG PET/MRI
STATISTICAL CONSIDERATIONS	• Per patient: concordance in cases, concordance in controls, sensitivity, specificity, positive predicted value, negative predictive value • Per lesion: distribution of lesions seen on each modality

SCHEMA


Eligible participant diagnosed with breast/prostate cancers and had ^{99m}Tc MDP bone scanning
^{18}F NaF/^{18}F FDG PET/WBMRI
12 months follow-up

LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Include additional abbreviations as needed. Remove any unnecessary abbreviations.

MDP	Methylene diphosphonate
FDG	Fluorodeoxyglucose
IRB	Institutional Review Board
IV	Intravenous
PET/MRI	Positron emission tomography – magnetic resonance imaging
SPECT/CT	Single photon emission computed tomography – computed tomography
RECIST	Response evaluation criteria in solid tumors
EORTC	European organization for research and therapy in cancer
ROC	Receiver-Operative-Characteristic
SUV	Standard Uptake Value

1. OBJECTIVES

1.1. Primary Objective

Testing the hypothesis that the combined ^{18}F NaF/^{18}F FDG PET/MRI, either alone or in combination, provide improved diagnostic accuracy over ^{99m}Tc MDP bone scanning

1.2. Secondary Objectives

- Evaluating the combined ^{18}F NaF/^{18}F FDG PET/MRI as a reliable bone scanning modality
- Evaluating the performance and reliability of the proposed WBMRI sequences: IDEAL and eDWI
- Evaluating a fast MRI protocol (2:30 min/bed)

2. BACKGROUND

2.1 Clinicaltrials.gov compliance

The FDA has approved all imaging scanners. This study has been registered on clinicaltrials.gov (NCT00375830).

2.2 Rationale

Fluorine-18 Fluorodeoxyglucose (^{18}F FDG) PET/CT is established as a powerful imaging tool for cancer detection and monitoring response to therapy. However, not all cancers are identified reliably due to variable rates of glucose metabolism. Whole-body MRI (WBMRI) emerges currently as an excellent modality for morphological characterization of soft tissue and skeletal lesions. Sodium Fluorine-18 (^{18}F NaF) was used in the 1970's for bone scanning and can be used as a skeletal tracer in current PET/CT scanners. The direct comparison of combined ^{18}F NaF/^{18}F FDG PET/CT and WBMRI for skeletal metastases detection was not attempted to date. However, such an approach has the potential to improve cancer diagnosis, staging, prognosis, and therapy monitoring. The combination of these technologies may also allow for improved screening or earlier cancer detection. Expanding on our prospective data from a preliminary pilot phase trial (10 subjects) comparing WBMRI, separate ^{18}F NaF PET/CT and separate ^{18}F FDG PET/CT, as well as on the pilot trial (56 participants at Stanford) of the combined ^{18}F NaF/^{18}F FDG PET/CT, we will now attempt a prospective study comparing these imaging modalities against themselves and against conventional ^{99m}Tc MDP bone scintigraphy.

2.3 Preliminary results

To date we have prospectively evaluated in a pilot phase trial (Sep 2007 – Oct 2008) 10 patients with cancer diagnosis, referred for ^{99m}Tc MDP bone scanning. There were 5 men and 5 women, 47 - 81 year-old (average: 61.5 ± 12), recruited for further imaging with ^{18}F NaF PET/CT, ^{18}F FDG PET/CT and WBMRI. All 4 scans were performed within 1 month for each participant. Lesions detected with each test were tabulated and results were compared. The image quality and evaluation of extent of disease was superior by ^{18}F NaF PET/CT over ^{99m}Tc-MDP scintigraphy in all patients with skeletal lesions and

over ^{18}F FDG PET/CT in 3 of the patients with skeletal metastases. ^{18}F NaF PET/CT showed osseous metastases where ^{18}F FDG PET/CT was negative in another 3 participants. Extra-skeletal metastases were identified by ^{18}F FDG PET/CT in 6 participants. WBMRI with the combination of IDEAL, STIR and DWI pulse sequences showed less lesions than ^{18}F NaF PET/CT in 5 patients, same number of lesions in 2 patients and more lesions in 1 patient. When compared to ^{18}F FDG, WBMRI showed fewer lesions in 3 patients and same lesions in 6 patients. Our pilot phase prospective trial demonstrated superior image quality and evaluation of skeletal disease extent with ^{18}F NaF PET/CT over ^{99m}Tc-MDP scintigraphy and ^{18}F FDG PET/CT, as well as the feasibility of multi-sequence WBMRI. In addition, ^{18}F FDG PET/CT provided valuable soft tissue information that can change disease management. Further evaluation of these findings using the recently introduced PET/MRI scanners is warranted.

In another prospective trial we demonstrated the non-inferiority of the combined ^{18}F NaF/^{18}F FDG PET/CT when compared to separate ^{18}F NaF PET/CT and ^{18}F FDG PET/CT scans for evaluation of cancer patients. This strategy of combining 2 PET radiopharmaceuticals in a single scan opens the possibility for improved patient care and reduction in healthcare costs due to a reduction in the number of scans being conducted.

In another 30 patients we have shown superior evaluation of skeletal disease extent with the combined ^{18}F NaF/^{18}F FDG PET/CT and the WBMRI compared to ^{99m}Tc-MDP scintigraphy. Further, PET/CT and WBMRI detected extra-skeletal disease that may change the management of these patients. A combination of ^{18}F NaF/^{18}F FDG PET and WBMRI may provide the most accurate staging of patients with breast and prostate cancers.

The recent introduction of hybrid PET/MRI scanners in clinical practice showed promising initial results for several clinical scenarios. More than a decade ago, multimodality imaging was introduced into clinical routine with the development of the PET/CT. Since then, PET/CT has been widely accepted in clinical imaging and has emerged as one of the main cancer imaging modalities. With the recent development of combined PET/MRI systems for clinical use, a promising new hybrid imaging modality is now becoming increasingly available. The combination of functional information delivered by PET with the morphologic and functional imaging of MR imaging (e.g., diffusion-weighted imaging, dynamic contrast-enhanced MR imaging and MR spectroscopy) offers exciting possibilities for clinical applications as well as basic research. However, the differences between CT and MR imaging are fundamental. This also leads to distinct differences between PET/CT and PET/MRI not only regarding image interpretation but also concerning data acquisition, data processing and image reconstruction. PET/MRI is expected to show advantages over PET/CT in clinical applications in which MRI is known to be superior to CT due to its high intrinsic soft tissue contrast. Two of these clinical indications are breast and prostate cancers.

80 subjects were enrolled to compare ^{18}F NaF/^{18}F FDG PET/MRI and the to ^{99m}Tc-MDP scintigraphy. Our results indicate that the ability of ^{18}F NaF/^{18}F FDG PET/MRI to identify more skeletal lesions than ^{99m}Tc-MDP BS, and to additionally

identify extra-skeletal disease, represents a beneficial alternative to the single modalities performed separately. ^{18}F NaF/^{18}F FDG PET/MRI is a promising approach for evaluation of skeletal and extra-skeletal lesions in a selected population of breast and prostate cancer patients. However, the current duration of exam (4 min/bed) is too long for some of the elderly patients. Therefore, we are now shortening the WBMRI protocol from 4 min/bed to 2:30 min/bed, reducing the total time from approximately 45 min/scan to 20-25 min/scan. We plan to enroll and have funding 50 additional subjects (25/year) to further evaluate the combined ^{18}F NaF/^{18}F FDG PET/MRI as a reliable bone scanning modality.

2.4 Study Design

We intend to perform a prospective trial to determine the role of the combined ^{18}F NaF/^{18}F FDG PET/MRI in the evaluation of skeletal metastases in patients with breast and prostate cancers. This study will be a comparative study that will investigate different types of bone scanning techniques. Patients will undergo preliminary evaluations to ensure eligibility, receive and sign informed consent, be enrolled in the trial, and then undergo the combined ^{18}F NaF/^{18}F FDG PET/MRI. Patients will be followed clinically by 12-months post scan evaluation.

Patients who present to the Nuclear Medicine and Molecular Imaging Clinic for a ^{99m}Tc MDP bone scan as part of their routine disease work-up/standard of care will be asked to participate in this study. If agreeable, written informed consent will be obtained by a member of the research team after explaining the risks, benefits, and procedures of the study. We will follow Stanford guidelines for screening patients for renal function prior to PETMRI if they are getting contrast. All scans will be performed within a 1-month timeframe. Blind interpretation of the combined ^{18}F NaF/^{18}F FDG PET/MRI will be performed by Nuclear Medicine and Radiology readers. A direct comparison for each detected lesion will be performed among the imaging modalities.

We will attempt to recruit patients who are referred for a ^{99m}Tc MDP bone scan for detection of skeletal metastases. In a typical year, approximately 3,500 ^{99m}Tc bone scans are performed in our Clinic, 90% (3,150) of them with referral for osseous metastases identification. We plan to recruit 40 patients per year for 2 consecutive years. Cancers with highest potential to metastasize to the skeleton (breast and prostate cancers) will be considered.

All age ranges of adult population (>18-year-old) will be recruited. Both men and women will be recruited. All ethnic background will be recruited. No healthy volunteers will be recruited. Pregnant women will be excluded because of the risk posed by unnecessary radiation to the fetus. Patients with metallic implants (prosthesis, ICD, pacemakers) will be excluded since these are contraindications for MRI.

The subjects will be paid $150 to participate in this protocol. No costs will be charged to the subjects.

3. PARTICIPANT SELECTION AND ENROLLMENT PROCEDURES

3.1 Inclusion Criteria

- Patient is ≥ 18 years old at the time of the drug administration
- Patient provides written informed consent
- Patient is diagnosed with ≥ stage 3 breast cancer or ≥ stage 2 prostate cancer (and/or PSA >10 micrograms/L), including patient with recurrent breast or prostate cancer
- Patient is scheduled to undergo a conventional bone scan
- Patient is capable of complying with study procedures
- Patient is able to remain still for duration of imaging procedure (about one hour)

3.2 Exclusion Criteria

- Patient is < 18 years old at the time of the drug administration
- Patient is participating in other research protocols at the time of the NaF/FDG PETMRI scan
- Patient is pregnant or nursing
- Metallic implants (contraindicated for MRI)
- Renal function impairment preventing administration of MRI contrast

3.3 Informed Consent Process

All participants must be provided a consent form describing the study with sufficient information for participants to make an informed decision regarding their participation. Participants must sign the IRB approved informed consent prior to participation in any study specific procedure. The participant must receive a copy of the signed and dated consent document. The original signed copy of the consent document must be retained in the medical record or research file.

3.4 Study Timeline

Primary Completion:
It will take 2 years for the study to reach "Primary Completion" from once the study opens to accrual of the additional 50 participants.

Study Completion:
It will take 3 years for the study to reach "Study Completion" from once the study opens to accrual.

4. STUDY AGENT INFORMATION

4.1 Study Agent

- Radiopharmaceutical: combination of ^{18}F NaF/^{18}F FDG
- Dose: ^{18}F NaF = 1 mCi; ^{18}F FDG = 4 mCi

4.2 Availability

Molecular Imaging Program at Stanford
Lucas Cyclotron Radiochemistry Facility
1201 Welch Road, Room PS049
Stanford, CA 94305-5484

4.3 Agent Ordering

Ordered in Radiology Information System (RIS)

4.4 Agent Accountability

RIS is password protected and part of the electronic medical records.

5. IMAGING SPECIFICS

5.1 Modality or Modalities to be used

PET/MRI

5.2 Details of Imaging (i.e. dynamic, static, number of scans, etc.)

Whole-body (head to toes) PET/MRI images will be obtained using a GE SIGNA scanner (GE Healthcare). The PET emission scan is corrected using segmented attenuation data of the MRI scan. The PET images are reconstructed with a standard iterative algorithm (OSEM, two iterative steps, 28 subsets) using GE software release 5.0. All images are reformatted into axial, coronal, and sagittal views and viewed with the software provided by the manufacturer (AW, GE Medical Systems).

PET/MRI images will be acquired in 3D mode at 45-60 minutes after injection of 4 mCi of ^{18}F FDG and 1 mCi of ^{18}F NaF, using 7-10 bed positions, 2:30 minutes/bed.

5.3 Details of processing/analysis

The PET/MRI scans will be interpreted by 2 ABNM certified Nuclear Medicine physicians (Andrei Iagaru, Guido Davidzon) and 2 ABR certified Radiologists (Andreas Loening, Shreyas Vasanawala) with significant clinical experience, blinded to the subjects' medical history and the results of other imaging modalities. The outcomes of the imaging methods will be analyzed and compared against each other. Consensus read will be obtained for each scan. Characterization of lesions as true positive, true negative, false positive or false negative will be done through a combination of clinical follow up, imaging follow-up and/or histopathology findings (when possible). For purposes of this study, the investigators will document an overall diagnosis of the findings for each scan on a 5 point scale to permit a receiver operating characteristic (ROC) analysis (1=benign, 2=likely benign, 3=uncertain, 4=likely malignant, 5=malignant). If the diagnosis is positive for metastases on any of the scans, the investigator will identify the number of lesions and locations of positivity, and record this information.

6. STUDY PROCEDURES & DETAIL

6.1 Criteria for Removal from Study

The Protocol Director may withdraw subjects from the study for one or more of the following reasons: failure to follow the instructions of the Protocol Director and/or study staff; determination that continuing the participation could be harmful to the subject; the study is cancelled or other administrative reasons.

6.2 Alternatives

The alternative is to not participate in the study.

7. STUDY CALENDAR

	Pre-Study	Wk 1	Wk 2	Wk 3	Wk 4	12 Months
Imaging scans done within 1 month of each other		---------->				
Informed consent	X					
Demographics	X					
Medical history	X					
Post-Scan Follow up						X

8. ADVERSE EVENTS AND REPORTING PROCEDURES

8.1 Potential Adverse Events

Risks associated with Participation

The administration of the radioactive substance will feel like a slight pinprick if given by intravenous injection. Patients who are claustrophobic may feel some anxiety while positioned in the scanner. Also, some patients find it uncomfortable to hold one position for more than a few minutes. The subjects will not feel anything related to the radioactivity of the substance in their body. Because the radioactivity is very short-lived, the radiation exposure is low. The substance amount is so small that it does not affect the normal processes of the body.

The average effective patient dose from whole-body ^{18}F-FDG PET examinations is about 25 mSv independent of the acquisition protocol preferred (Brix G, Lechel U, Glatting G, Ziegler SI, Munzing W, Muller SP, Beyer T.Radiation exposure of patients undergoing whole-body dual-modality 18F-FDG PET/CT examinations. J Nucl Med. 2005 Apr;46(4):608-13). The bladder wall receives an average of 440 mrad/mCi (s.e. 76) in ten subjects who voided at 2 hr after administration of tracer. If these subjects had voided at 1 hr, the bladder-wall dose would have been reduced to 220 mrad/mCi. The brain received an average of 81 mrad/mCi in eight subjects. The doses to other organs, calculated from published dog biodistribution data, are between 50 and 85 mrad/mCi except for spleen and heart, which both received 160 mrad/mCi (Jones SC, Alavi A, Christman D, Montanez I, Wolf AP, Reivich M. The radiation dosimetry of 2 [F-18]fluoro-2-deoxy-D-glucose in man. J Nucl Med. 1982 Jul;23(7):613-7).

Fluorine ions are a normal body constituent. The amount of fluorine ions in Sodium Fluoride F 18 Injection at the indicated dose has minimal effect on normal human physiology. When F-18 injection was approved for marketing in 1972, no adverse reactions were noted in over 400 patient studies reported in the medical literature. In a 1999 review of the published literature, publicly available reference sources and adverse drug reaction reporting systems indicated that adverse reactions have not been reported for F-18 injection. Fluorine-18 ions decay with a physical half-life of 109.7 minutes. Ninety-seven percent (97%) of the decay results in emission of a positron with a maximum energy of 0.635 MeV, and 3% of the decay results in electron capture with subsequent emission of characteristic X-rays of oxygen. The bone and bone marrow are considered the target and critical organs. These estimates were calculated based on human data and using the data published by the International Commission on Radiological Protection for Sodium Fluoride F-18 injection.

Side effects of the MRI contrast agent injection include mild headache, nausea and local pain. Rarely (less than 1% of the time) low blood pressure and lightheadedness occurs. This can be treated immediately with intravenous fluids. Very rarely (less than one in one thousand), patients are allergic to the contrast agent. These effects are most commonly hives and itchy eyes, but more severe reactions have been seen which result in shortness of breath.

8.2 Adverse Event Reporting

We do not anticipate hazardous situations for the subjects as a result of this protocol. However, procedures will be in place for verification of correct radiopharmaceutical dose and route of administration (i.e., each dose will be double checked for dosimetry and quality by a researcher and technologist). The study Principal Investigator (PI) or his designee will report unanticipated AEs related to the Stanford CCTO Safety Coordinator within 10 working days of becoming aware of the event (5 days if the event is life-threatening or resulted in death) using the Adverse Events Communication Form. If the principal investigator determines the unanticipated adverse device effect presents an unreasonable risk to subjects, the study will be terminated as soon as possible, but no later than 5 working days after the PI makes the determination and no later than 15 working days after first receiving notification of the effect.

9. REGULATORY CONSIDERATIONS

9.1 Institutional Review of Protocol

The protocol, the proposed informed consent and all forms of participant information related to the study (e.g. advertisements used to recruit participants) were reviewed and approved by the Stanford IRB. Any changes made to the protocol will be submitted as a modification and will be approved by the IRB prior to implementation. The Protocol Director will disseminate the protocol amendment information to all participating investigators.

9.2 Data Management Plan

Study data, patients' medical records, and eCRFs will be monitored in accordance with Stanford standard operating procedures (SOPs), and the respective national or regulatory government regulations. The investigator will be responsible for monitoring the safety of subjects who have enrolled in the study. The Stanford Data Safety Monitoring Committee (DSMC) will also monitor the study annually. The Stanford Cancer Institute Data and Safety Monitoring Committee (DSMC) will audit study related activities at least annually in **accordance with the DSMC SOP** to determine whether the study has been conducted in accordance with the protocol, local standard operating procedures, FDA regulations, and Good Clinical Practice (GCP). This may include review of regulatory binders, case report forms, eligibility checklists, and source documents. In addition, the DSMC will regularly review serious adverse events and protocol deviations associated with the research to ensure the protection of human subjects. Results of DSMC audits will be communicated to the IRB and the appropriate regulatory authorities at the time of continuing review, or in an expedited fashion, as needed.

10. STATISTICAL CONSIDERATIONS

10.1 Populations

Patients with ≥ stage 3 breast cancer or ≥ stage 2 prostate cancer (and/or PSA >10 micrograms/L), including patients with recurrent breast or prostate cancer will be enrolled. The analysis subset will consist of patients with an interpretable ^{99m}Tc MDP

bone scan, ^{18}F NaF/^{18}F FDG PET/MRI evaluations, and a known clinical bone lesion evaluation at 12 months.

10.2 Key Variables

Diagnostic bone metastases status using ^{99m}Tc MDP bone scan, ^{18}F NaF/^{18}F FDG PET/MRI, bone metastases status at 12 months (all binary)

10.3 Endpoints

Primary: concordance between ^{99m}Tc MDP bone scan and ^{18}F NaF/^{18}F FDG PET/MRI, as the proportion of patients where the modalities agree.

Secondary:

- Per patient: concordance in cases, concordance in controls, sensitivity, specificity, positive predicted value, negative predictive value
- Per lesion: distribution of lesions seen on each modality
- Proportion of diagnostic quality scans using the faster protocol compared to first cohort of 80 participants

10.4 Plan of Analysis

The principal analysis will aggregate patients from the two groups and will be conducted on a per-patient basis. We will calculate the concordance between the modalities across outcomes (combining cases and controls) and evaluate the results by calculating the kappa coefficient. Secondary endpoints will be calculated, both as aggregates of the three diseases and separately by disease. Sensitivities and other summaries will only be calculated if they involve a denominator of at least 10.

10.5 Sample Size

A key parameter in determining the sample size for a study of the sensitivity and specificity of a new diagnostic modality relative to a standard modality is the degree of concordance of the modalities, or roughly speaking, the degree to which the modalities are correlated. The higher the concordance, the smaller the sample size required. For example, if current modalities for bone metastases detection (^{99m}Tc MDP bone scan) have a sensitivity of 80%, then the number of cases needed to demonstrate a 10% margin of superiority ranges from 83 to 284. Details are given in the Appendix

10.6 Interim Analyses

No interim analyses are planned.

10.7 Criteria for Future Studies

The accrual will continue until reaching the sample size required for statistical analysis, as described above, given the results from the previous 30 patients. The combined PET/MRI scanners are an ideal tool to evaluate this hypothesis.

10.8 Accrual estimates

We will attempt to recruit patients who are referred for a ^{99m}Tc MDP bone scan for

detection of skeletal metastases. In a typical year, approximately 3,500 ^{99m}Tc bone scans are performed in our clinic, 90% (3,150) of them with referral for osseous metastases identification. We plan to recruit 40 patients per year. Cancers with highest potential to metastasize to the skeleton (breast and prostate cancers) will be considered.

11. APPENDIX

The sample size follows Connett et al 1 . We replace the nomenclature of "Control" by "Old modality" and "Case" by "New Modality". The numbers A, B,C D are the true probabilities summing to 1 as shown in the table:

	Old Modality		
New Modality	Positive	Negative	
Positive	A	B	Se.New
Negative	C	D	
	Se.Old		1

A convenient parametrization consists of

- The proportion discordant $K = B + C$
- the sensitivity of the old modality Se.Old=$A+C$,
- the target improvement in sensitivity $\Delta = (A + B) - (A + C) = B - C$

Connett et al adopt the parameterization:

- Odds ratio $\psi = B/C$
- Proportion positive under old but negative under new $P_{01} = C = (K + \Delta)/(K - \Delta)$

With this parametrization the sample size is given by

$$n = \frac{\left(z_\alpha \sqrt{\psi + 1} + z_\beta \sqrt{\psi + 1 - (\psi - 1)^2 P_{01}}\right)^2}{(\psi - 1)^2 P_{01}}$$

The Connett parameters can be derived thus:

$$P_{01} = (K - \Delta)/2 \text{ and } \psi = (K + \Delta)/(K - \Delta)$$

To illustrate, we set the sensitivity of the old modality to 0.8, Delta to 0.1, If we set the discordance close to its minimum value 0.11 we get the following table:

	Old Modality		
New Modality	Positive	Negative	
Positive	**0.795**	**0.105**	**0.900**
Negative	**0.005**	**0.095**	**0.100**
	0.800	**0.200**	**1.000**

With resulting OR=21, P01=0.005. With these parameters Connett's formula give N=84.

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1 Connett, J. E., Smith, J. A., & McHugh, R. B. (1987). Sample size and power for pair-matched case-control studies. *Statistics in Medicine*, *6*, 53-59.

If we set the discordance to 0.3 (maximum attainable with the other constraints) we get the table

	Old Modality		
New Modality	Positive	Negative	
Positive	**0.700**	**0.200**	**0.900**
Negative	**0.100**	**0.000**	**0.100**
	0.800	**0.200**	**1.000**

With resulting OR=2 P01=0.1, and the Connett formula gives a sample size of 233

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STANFORD UNIVERSITY Participant Eligibility Checklist		**Version 9: 28 June 2017**
Protocol Director:	Andrei Iagaru, M.D. eProtocol: 3778	
Protocol Title: Combined 18F NaF/18F FDG PET/MRI for Detection of Skeletal Metastases		

Inclusion Criteria (From IRB approved protocol)	**Yes**	**No**	**N/A**	**Supporting Documentation**
1. Patient is ≥ 18 years old at the time of the drug administration	☐	☐	☐	☐
2. Patient provides written informed consent	☐	☐	☐	☐
3. Patient is diagnosed with ≥ stage 3 breast cancer or ≥ stage 2 prostate cancer (and/or PSA >10 micrograms/L), including patient with recurrent breast or prostate cancer	☐	☐	☐	☐
4. Patient is scheduled to undergo a conventional bone scan	☐	☐	☐	☐
5. Patient is capable of complying with study procedures	☐	☐	☐	☐
6. Patient is able to remain still for duration of imaging procedure (about one hour)	☐	☐	☐	☐

Exclusion Criteria (From IRB approved protocol)	**Yes**	**No**	**N/A**	**Supporting Documentation**
1. Patient is < 18 years old at the time of the drug administration	☐	☐	☐	☐
2. Patient is participating in other research protocols at the time of the NaF/FDG PETMRI scan	☐	☐	☐	☐
3. Patient is pregnant or nursing	☐	☐	☐	☐
4. Metallic implants (contraindicated for MRI)	☐	☐	☐	☐
5. History of renal insufficiency	☐	☐	☐	☐

*All subject files must include supporting documentation to confirm subject eligibility. The method of confirmation can include, but is not limited to, laboratory test results, radiology test results, subject self-report, and medical record review.

Statement of Eligibility

By signing this form of this trial I verify that this subject is [☐ **eligible** / ☐ **ineligible**] for participation in the study. This study is approved by the Stanford Cancer Institute Scientific Review Committee, the Stanford IRB, and has finalized financial and contractual agreements as required by Stanford School of Medicine's Research Management Group.

Signature:	Date:
Printed Name:	

Signature:	Date:
Printed Name:	

Signature:	Date:
Printed Name:	