The Effect of Rapid Acquisition Myocardial Perfusion Imaging on Improving the Diagnosis of Coronary Artery Disease

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A. Study Purpose and Rationale

The prevalence of coronary artery disease has been estimated to affect approximately 13.7 million Americans [1]. There are a variety of non-invasive modalities for the diagnosis of coronary artery disease, one of which includes using SPECT MPI (single-photon emission CT myocardial perfusion imaging). In a meta-analysis, the diagnostic accuracy of SPECT compared to coronary angiography (the current gold standard for diagnosis), demonstrated a Se 88% and Sp 77% in 10 studies of 1174 patients who had undergone either exercise or pharmacologic SPECT [2].

It is estimated that over 6 million patients a year have a SPECT myocardial perfusion study [3]. Given the increased utilization of SPECT perfusion imaging as a diagnostic test in the setting of a limited number of SPECT cameras, there has been growing interest in improving the efficiency of such tests. Currently, the SPECT protocol requires sufficient time for an exercise or pharmacologic stress, isotope injection, and patient positioning on the scanner followed by image acquisition, which takes approximately 30 minutes. While certain aspects of the stress protocol are fixed, newly developed hardware (cameras) and software reconstruction algorithms claim that images can be acquired in half the amount of time.

Reducing image acquisition time has several benefits. From a patient safety standpoint, it reduces the exposure to radiation from the CT scanner. Furthermore, diagnostic accuracy could be improved by a reduced frequency of motion artifacts (breathing, patient motion, cardiac motion). Lastly, a diagnostic center will be able to perform more imaging tests in a day, thus, becoming more efficient.

Our institution acquired the Phillips Precedence SPECT/CT 16 slice scanner, whose manufacturer claimed that, along with Astonish 3D reconstruction, rapid-acquisition imaging would be possible. In preliminary studies, we constructed anthropomorphic cardiac phantoms with fixed defects of different sizes and severity to create a model for coronary artery disease. We imaged the cardiac phantom using the standard protocol (30 second/frame) and the short protocol (15 second/frame) and used the resulting perfusion images to determine the volume of the infarct. Comparing the volumes obtained in the standard/short protocol to the actual volume of the defect, we were able to show that the short protocol was able to detect the infarct with sufficient accuracy (unpublished data).

Given the promising preliminary results, the next step was to see if the diagnostic accuracy of rapid acquisition could be extended to a patient population. This study can be performed retrospectively on individuals who have already had stress tests in this laboratory since the raw data can be processed in both standard and short

protocol mode without reimaging the patient. To obtain data for the short protocol mode, every other second would be removed from the data set on a frame, thus simulating a 15 second/frame. While this is not identical to an actual 15 second/frame (since every alternate second from the scan is removed), it is a very close approximation. Should this study prove that the short protocol retains the diagnostic accuracy of the standard protocol for the diagnosis of CAD, this can serve as validation for a subsequent study in which the patient is actually imaged under the short protocol (as opposed to a simulated short protocol through data processing). Given that coronary angiography is the definitive diagnostic test for the presence of CAD, it will serve as the gold standard to which to compare the accuracy of the SPECT (both short/long protocol).

We hypothesize that it the short protocol will be noninferior to the standard protocol for the detection of CAD.

B. Study Design and Statistical Analysis

This is a retrospective study. The study subjects are drawn from a database of those individuals who had cardiac catheterizations at CPMC between the years of Jan 2005-Jan 2008. Subjects must have had an exercise nuclear stress SPECT test performed at CPMC within the 2 weeks prior to the catheterization and meet predefined inclusion/exclusion criteria will be included in the study (see **Study Subjects**). To reduce variability, the myocardial perfusion SPECT must have been performed as an exercise stress (as opposed to pharmacologic). Furthermore, only stress images (not rest images) will be analyzed.

The raw data from subjects' corresponding SPECT scans will be processed with the short protocol (15 second/frame). A panel of nuclear cardiologists will be responsible for reading the short protocol acquisitions. Based on a 17 segment stress score (see **Appendix 1**), 17 segments of LV will be scored from 0 to 4 (0= normal uptake, 1= mild decrease in uptake, 2= moderate decrease in uptake, 3= severe decrease in uptake, 4= absent uptake). Segments 1, 2, 7, 8, 13, 14 will be assigned to the region of the LAD; segments 3, 4, 9, 10, 15 will be assigned to the region of the RCA, and segments 5, 6, 11, 12 will be assigned to the region of the LCx. This scoring system allows for assessment of severity and extent of perfusion defects [4,5]. An abnormal coronary territory was defined as >=1 segment with stress score >=2 in the segments. This is the same scoring system that was used for standard protocol at the time the test was initially performed. Thus, the prior reads from the standard protocol will be compared to the reads of the short protocol. For angiography, CAD was defined in a particular region if >=50% stenosis [6]. For example, if cardiac catheterization shows disease in RCA, but no disease in LCx and LAD, for the stress test to be "right", it must show disease only in the RCA, but no disease in LCx/LAD based on the aforementioned criteria.

An evaluation of non-inferiority will be conducted, asserting that the short-protocol is non-inferior to the standard-protocol. For example, assume the cardiac cath showed disease only in the RCA. The inferiority proportion would be cases where the short protocol is wrong and the standard protocol is accurate (ie: if standard protocol showed a defect in the RCA, but no other coronary artery and short protocol either

showed an RCA defect in addition to another defect, or failed to show a defect in RCA). The superiority proportion would be cases where the short protocol is right and the standard protocol is wrong. Assuming that non-inferiority for short protocol is defined by an inferiority proportion <5 % (that is, out of n subjects, <5% are cases where short protocol was less accurate than standard protocol). However, based on prior phantom studies, we can postulate that the inferiority proportion is 0%, leading to an n=95 on one-sided chi-squared power analysis (assuming alpha 0.05 and power of 0.80),

C. Study Procedure

Since this is a retrospective study, the only procedure is that the short-protocol scans will be read by a panel of nuclear cardiologists.

D. Study Drugs

Not applicable.

E. Medical Device

Not applicable.

F. Study Subjects

The study subjects are drawn from a database of those individuals who had cardiac catheterizations at CPMC between the years of Jan 2005- Jan 2008. Subjects will be between the ages of 50-80, and must have had an exercise nuclear stress SPECT test performed at CPMC within the 2 weeks prior to the catheterization.

Subjects will be excluded if they have had prior cardiac surgery (including CABG, valve repair/replacement), history of coronary artery revascularization prior to the catheterization, cardiac catheterization indicated that they were left coronary artery dominant, or myocardial perfusion SPECT was reported as an inadequate study.

G. Recruitment of Study Subjects

No subjects will be recruited for this study, as the database already exists.

H. Confidentiality of Study Data

To ensure confidentiality of participants, all data will be coded a unique code number. Data will be stored in a secure location, accessible only to the investigators.

I. Potential Conflict of Interest

There are no potential conflicts of interests for the study investigators.

J. Location of Study

The study will be carried out at New York-Presbyterian Hospital Columbia Campus in New York City. Diagnostic cardiac catheterizations took place in the Interventional Cardiology suite at Presbyterian Hospital . The myocardial perfusion imaging took place in the Phillips Precedence SPECT/CT in the Nuclear Cardiology suite at Presbyterian Hospital.

K. Potential Risks

Since this is a retrospective study examining the data from subjects that have already had cardiac catheterizations and have already had myocardial perfusion imaging, study participants will not be subjected to any additional risk.

L. Potential Benefits

There are no benefits to the study subjects.

M. Alternative Therapies

There are no alternative therapies, as this is a retrospective study.

N. Compensation to Subjects

Patients will not be compensated for participation.

O. Costs to the Subjects

There will be no additional cost to patients.

P. Minors as Research Subjects

All patients below the age of 18 will be excluded from this study.

Q. Radiation

Subjects will not be exposed to any excess radiation, since this is a retrospective study.

R. REFERENCES

[1]. www.uptodate.com Peter Wilson, MD. Epidemiology and prognosis of coronary heart disease.

[2]. Garber, A et al. Cost-Effectiveness of Alternative Test Strategies for the Diagnosis of Coronary Artery Disease. *Ann Intern Med* 1999; 130:719-728.

[3]. Borges-Neto, S et al. Clinical results of a novel wide beam reconstruction method for shortening scan time of Tc-99m cardiac SPECT perfusion studies. *Jounral of Nuclear Cardiology* 2007; 14:555-65.

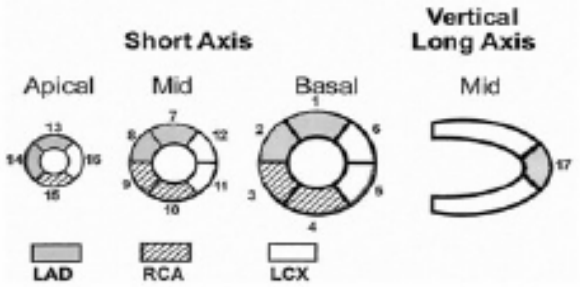
[4]. Cerqueira, M et al. Standardized Myocardial Segmentation and Nomenclature for Tomographic Imaging of the Heart: A Statement for Healthcare Professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. *Circuilation* 2002; 105: 539-542.

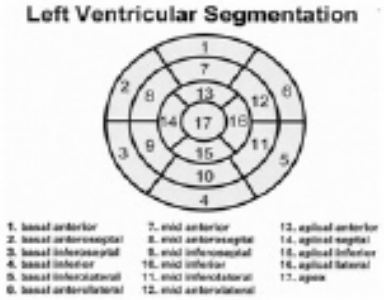
[5]. Heller, G. "Best-Practice SPECT Protocol for 2007: Case-based approach". New Approaches and Procedures in Office Based Nuclear Cardiology and Cardiac CT, Conference in Orlando, FL October 2007. Online ppt.

[6] Kang, Xingping et al. Myocardial Perfusion SPECT in Diabetes. *Am Heart J 1999*; 137(5): 949-957.

[7] Hansen, et al. Myocardial perfusion and function SPECT. *Journal of Nuclear Cardiology 2006;* 13:e97-120.

Appendix 1





0	Normal uptake
1	Mild decrease in uptake
2	Moderate decrease in uptake
3	Severe decrease in uptake
4	Absent uptake

SEGMENT	NON-ATTENUATION CORRECTED	
	STRESS SCORE	REST SCORE
1. Anterior		
2. Antero-septal		
3. Infero-septal		
4. Inferior		
5. Infero-lateral		
6. Antero-lateral		
7. Anterior		
8. Antero-septal		
9. Infero-septal		
10. Inferior		
11. Infero-lateral		
12. Antero-lateral		
13. Anterior		
14. Septal		
15. Inferior		
16. Lateral		
17. Apical		
SUMMED SCORE		

[4,5]