

# Myocardial Uptake of a Novel Tc-99m Labeled Glucose Analog (Tc-99m EC-DG) in Normal and Ischemic Subjects during Rest and Exercise Stress Testing

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## ABSTRACT

**INTRODUCTION:** Current Tc-99m tracers, such as Tc-99m sestamibi (MIBI), measure the presence of ischemia by indirectly measuring changes in myocardial blood flow. In this study, we examined the glucose analog: Tc-99m-labeled ethylenedicycysteine-deoxyglucose (<sup>99m</sup>Tc-EC-DG) as a potential "positive signal" tracer of myocardial ischemia with and with exercise stress testing.

**METHODS:** <sup>99m</sup>Tc-EC-DG is thought to utilize the GLUT 1 and 4 transporter receptors and should only be absorbed when ischemic changes are present in the myocardium. For this study, we sought to measure the uptake of <sup>99m</sup>Tc-EC-DG in normal volunteers and ischemic subjects (as determined by MIBI stress testing) during rest and exercise stress. We measured the signal to noise (STN) and signal to background (STB) in the normal myocardium and ischemic defects relative to the blood pool, liver, lung and soft tissue.

**DATA ACQUISITIONS:** Data were acquired in 13 subjects (12 male, 7 normal, 11 rest, 5 exercise abnormal) as a part of the Phase 1, <sup>99m</sup>Tc-EC-DG study (CP-TDS-C1). Subjects were first imaged using a standard, low dosage-high dosage exercise stress protocol using MIBI. Normal was reviewed to confirm subjects both determination of normalcy or abnormality. Subjects were then imaged on a Philips Cardio 60 within 14 days with 30 mCi of <sup>99m</sup>Tc-EC-DG at rest and within 14 days, using a modified Bruce treadmill protocol, administering another 30mCi of <sup>99m</sup>Tc-EC-DG.

**RESULTS:** In these normal subjects, the myocardial uptake was low and did not vary significantly (23% +/- 11% (R), 24% +/- 8% (EX) variations about mean myocardial uptake). In the 5 abnormal subjects, 6 ischemic defect were examined. For exercise stress, uptake of <sup>99m</sup>Tc-EC-DG achieved >2σ uptake in 3 of the defects, and >1σ in 5 of 6 defects. In addition, at rest uptake of <sup>99m</sup>Tc-EC-DG achieved >2σ uptake in 2 of the defects, and >1σ in 3 of 6 defects. Exercise defect size had a weak correlation with MIBI defect, and less correlation with rest. **CONCLUSION:** <sup>99m</sup>Tc-EC-DG was found to be absorbed by abnormal myocardial tissue when stimulate by exercise stress. Furthermore, <sup>99m</sup>Tc-EC-DG may have the potential for detecting ischemia in the absence of exercise in a significant fraction of patients.

## <sup>99m</sup>Tc-EC-DG

- <sup>99m</sup>Tc-ECDG is currently in Phase 2 studies in the United States and is not currently available for commercial distribution.
- <sup>99m</sup>Tc-ECDG is a Tc-99m labeled glucose analog
- Absorbed by cell that utilize the Glut-4 transporter pathway.
- Ischemic cells activate this pathway to provide cell-membrane and protein synthesis as a part of the cellular repair mechanism.
- Unlike FDG, Tc-EC-DG does not localize to inflammation.

## HYPOTHESIS

- <sup>99m</sup>Tc-EC-DG will localize to ischemic myocardium that has been stimulated using exercise
- <sup>99m</sup>Tc-EC-DG will demonstrate minimal or no uptake in normal myocardium.
- In some circumstances, it may be possible to detect <sup>99m</sup>Tc-EC-DG uptake at rest in patients with no history of exercise within the last 24 hours.

## PATIENT POPULATION

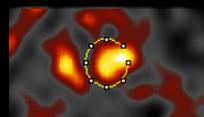
- 13 Subjects (12 male, 7 normal, 11 rest studies and 5 exercise) were recruited as a part of a Phase 1 clinical trial CP-TDS-01 of <sup>99m</sup>Tc-EC-DG.
- Abnormal patients had a reversible defect on a conventional two day exercise sestamibi study
- Normal patients were required to have a normal exercise treadmill test and a normal two day exercise sestamibi study.

## DATA ACQUISITIONS

- Early uptake measured using a series of 60x10sec acquired using a Spectrum Dynamics D-SPECT system
- Late uptake was measured using a conventional Anger SPECT system with attenuation correction (CARDIO-60 WITH VantagePRO):
  - 35 sec/stop @ 60 min (9 subjects) or (4 subjects);
  - 35 sec/stop @ 15 minutes
  - 35 sec/stop @ 75 minutes
- Reconstruction was AutoSPECT+

## DATA ANALYSIS

- Reconstructed volumes were analyzed using ImageJ (v1.4.3u) to draw quantitative ROIs
- Normal subjects:
  - Circular ROIs at the apex, mid-ventricle, and base of short axis oblique view.
  - ROI sampling = 12° intervals.
- Abnormal subjects:
  - Circular ROI through the defect on the SA view.
  - 1 patient, had an apical ischemic defect. An elliptical ROI was used from the HLA
  - ROI sampling = 12° intervals.
- Also measure the blood pool concentration (BPC)



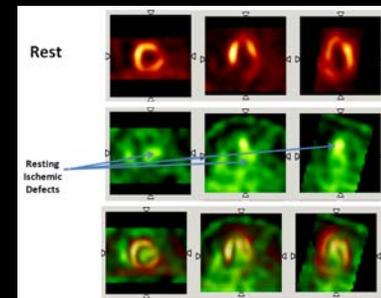
- Depth of a defects were measured using an equivalent width:

$$EAW = \sum_{i=\theta_0}^{\theta_1} \frac{C_i - C'_i}{\Delta \theta_i}$$

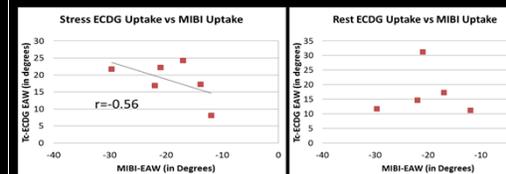
## RESULTS

- <sup>99m</sup>Tc-ECDG was not taken up by normal myocardium at rest or during exercise stress (23+/-11% (R), and 24%+/-8% (E))
- For exercise in abnormal subjects, 6 defects were observed in the sestamibi studies:
  - 3/6 defects were >2σ over background and 5/6 defects with >1σ over background.
  - In addition, at rest, <sup>99m</sup>Tc-EC-DG uptake achieved >2σ uptake in 2/6 of the defects, and >1σ in 3/6 defects.
  - There was a weak correlation between <sup>99m</sup>Tc-ECDG uptake and sestamibi deficit:

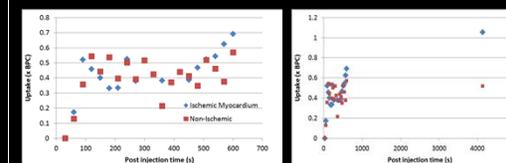
## RESULTS-cont.



<sup>99m</sup>Tc-ECDG resting uptake in CP0110



Uptake of <sup>99m</sup>Tc-EC-DG uptake vs MIBI defect size



<sup>99m</sup>Tc-EC-DG uptake begins at ~10 min post injection

## CONCLUSIONS

- <sup>99m</sup>Tc-ECDG is not taken up in normal myocardium at rest or as a result of exercise
- <sup>99m</sup>Tc-ECDG is taken up in abnormal as a result of exercise and in some cases at rest.
- The uptake of <sup>99m</sup>Tc-ECDG begins at ~10 minute post injection and continues for at least one hour