



Cardiospec™

Optimal Revascularization Therapy

Introduction

Management of patients with advanced coronary artery disease (CAD) is a major challenge for the cardiologist and cardiac surgeon. Patients with advanced CAD frequently have limited symptoms with recurrent angina, angina at low work thresholds, breathlessness, and other debilitating conditions. These patients have often been through several “re-do” coronary bypass procedures and multiple percutaneous coronary interventions.

Surgical and interventional options for these patients typically have been exhausted or will result in only partial revascularization. Therefore, therapy remains limited to the use of multiple anti-anginal medications, reduced activity, exertion, and stress level, and significant alteration and limitation of lifestyle.

The burgeoning field of therapeutic angiogenesis offers hope for these patients. The goal of this emerging approach is to therapeutically induce the growth and development of new vasculature in zones of severe ischemia in the myocardium, with the hope that new capillaries and arterioles generated will connect to remnant existing vasculature. These neovessels are viewed to act as collaterals, perfusing ischemic territories unapproachable by macro procedures such as angioplasty and bypass surgery.

Several strategies are being pursued for therapeutic angiogenesis. Local injection of naked DNA or viral vectors coding for various angiogenic growth factors (*eg*, VEGF and FGF) have been examined in animals and humans, as have local injections of actual growth factor proteins such as VEGF, FGF, and IGF. In addition, local delivery of endothelial cells and bone marrow-derived precursor stem cells are being studied.

While these approaches will ultimately provide insight into many basic mechanisms involved in myocardial angiogenesis, significant limitations exist with many of these as far as rapid translation into clinically useable therapies in the near term. Another strategy that has been examined for several years now, is that of injury-induced angiogenesis. While not referred to directly in the literature by this term, many studies have emerged over the years using variants of this approach. However, long term effect has not been demonstrated.

A new Non-Invasive Cardiac Angiogenesis Therapy (NI-CATH) was developed recently which couples the ability of low intensity shock waves to induce angiogenesis to the therapy of angina and is becoming a new alternative in the treatment of these patients. Reversible ischemic regions, no longer approachable or treatable by existing invasive methods are being targeted and treated with NI-CATH. Short and long term results have shown the ability of this new therapy to increase local perfusion, reduce symptoms and improve overall quality of life of patients.

For further information, please do not hesitate to contact me,

Gil Hakim
Cardio-Vascular Business Line Manager
Medispec Ltd, gil@medispec.com

Clinical results (submitted to the WCC 2006)

Non invasive Cardiac Angiogenesis shock wave therapy (NI-CATh) increases perfusion and exercise tolerance in endstage CAD patients

Achim Gutersohn⁽¹⁾, Ira Karoussos⁽¹⁾, Gil Hakim⁽²⁾, Sara Lammers⁽¹⁾, Raimund Erbel⁽¹⁾

⁽¹⁾Dep. Cardiology West German Heart centre, University of Essen, Germany ⁽²⁾Medispec, USA

Background:

Due to improved revascularisation methods survival of CAD patients has been increased over the years leading to the problem what to do with the increasing numbers of endstage CAD patients not eligible for CABG or PCI.

Different approaches have been tried out to induce myocardial angiogenesis. We here demonstrate a new non invasive Angiogenesis therapy using shock waves.

Shock wave therapy was applied in 25 patients. All had to have proven reversible ischemia in at least one myocardial area using SPECT.

Methods: 25 pts either with refractory angina (n=15) or chronic occlusion of one epicardial vessel (n=10) mean age $63,8 \pm 8,2$ years were treated with R-wave triggered shock waves (Cardiospec© shock wave applicator, MEDISPEC, USA) were applied using ultrasound to find the ischemic zone. About 3 x 900 impulses were applied to ischemic areas using energy of 0,1 mJ/mm². SPECT was performed at baseline and after 3 months follow up.

Results:

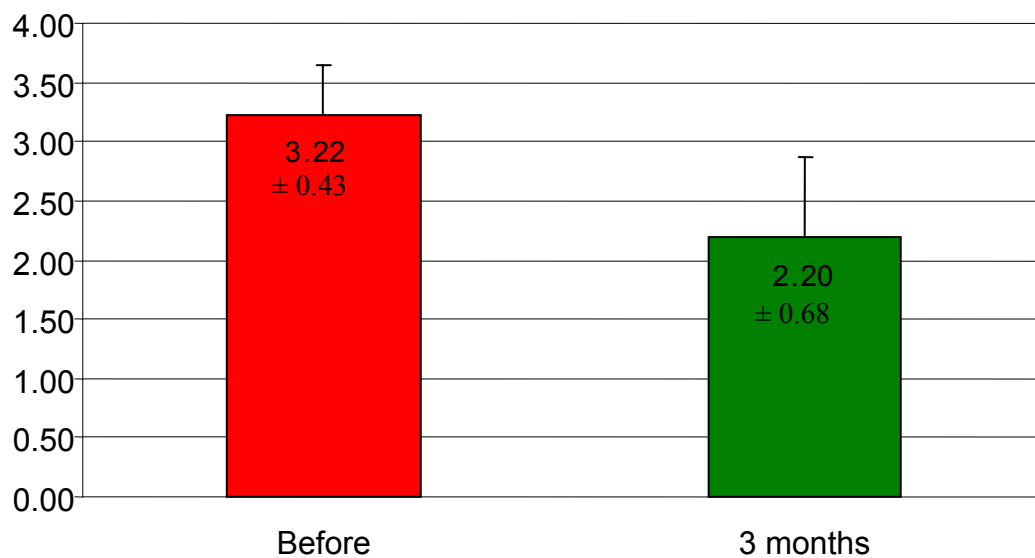
Therapy was well tolerated by all pts., no side effects were present, no arrhythmias, no cardiac enzyme rise, no new wall motion abnormality. Therapy could be easily performed in patients. CCS scale improved from baseline 3.22 ± 0.43 to 2.2 ± 0.68 ($p < 0.05$) after 3 months. Exercise tolerance was increased from 52.7 ± 24.08 watt to 86.5 ± 12.97 watt ($p < 0.05$). SPECT revealed a significant increase in myocardial perfusion using the 24 segment model only in treated myocardial areas.

Conclusion:

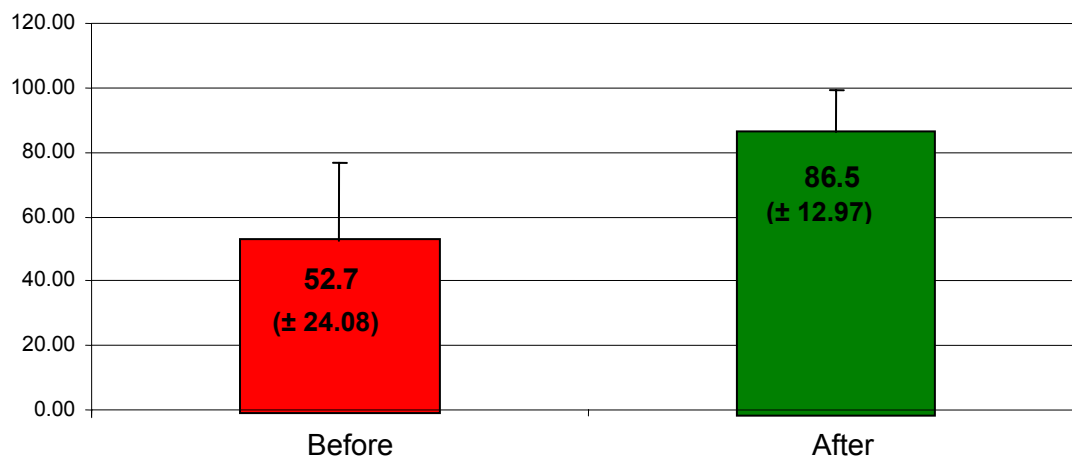
In vitro and animal data show an increase of angiogenic factors in the heart and peripheral muscle after shock wave treatment. We present clinical data on safety, feasibility and effectivity of the first pilot study using Cardiospec © shock wave applicator, in patients with myocardial ischemia.

This data shows that shock waves may be a non invasive alternative method in the treatment of myocardial ischemia in endstage CAD patients.

CCS class:



Exercise tolerance (watt):



Please find below further analysis of the results, detailing the effect of NI-CATH on this group of patients. The results represents 3 months follow-up.

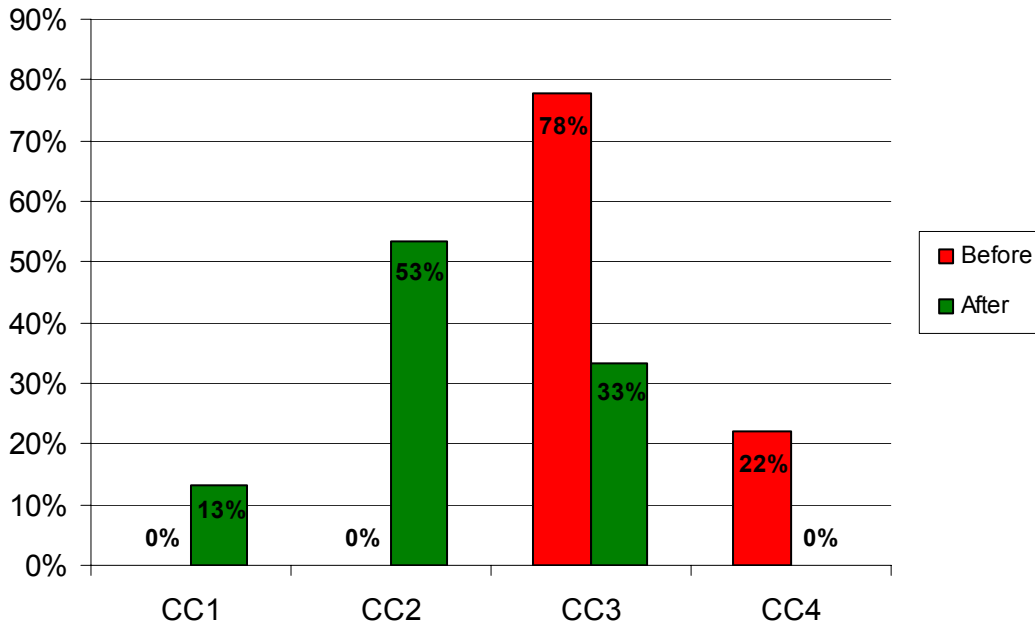


Figure A: Overall changes in CCS class before and after NI-CATH treatment. The figure shows a shift toward improved CCS class after NI-CATH treatment. No patients remain in CCS class IV after the treatment

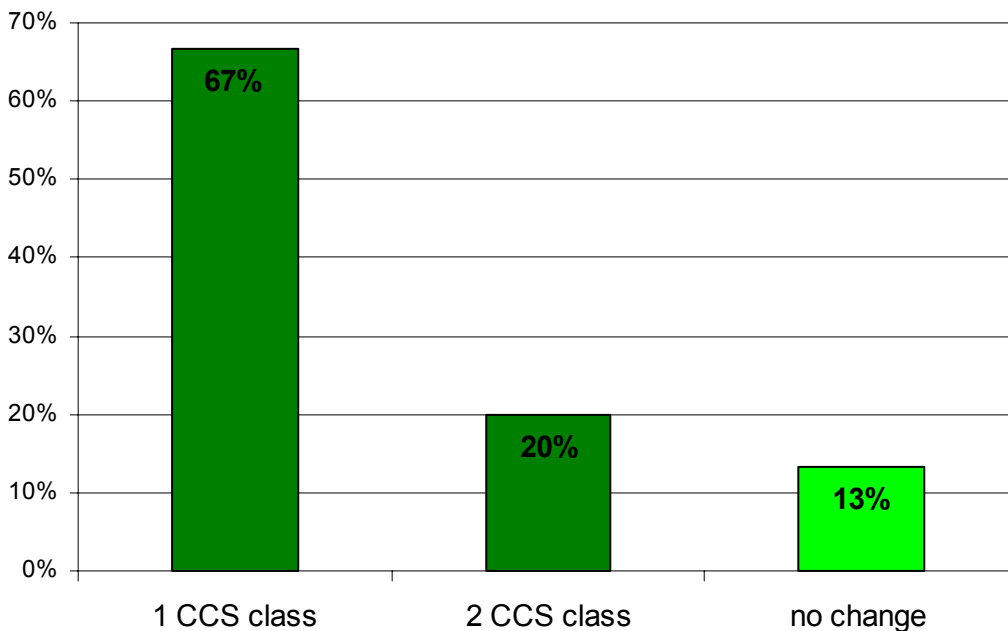


Figure B: The figure shows the percentage of patients who have improved in at least 1 CCS class. 20% of the patients reports an improvement of 2 CCS classes.

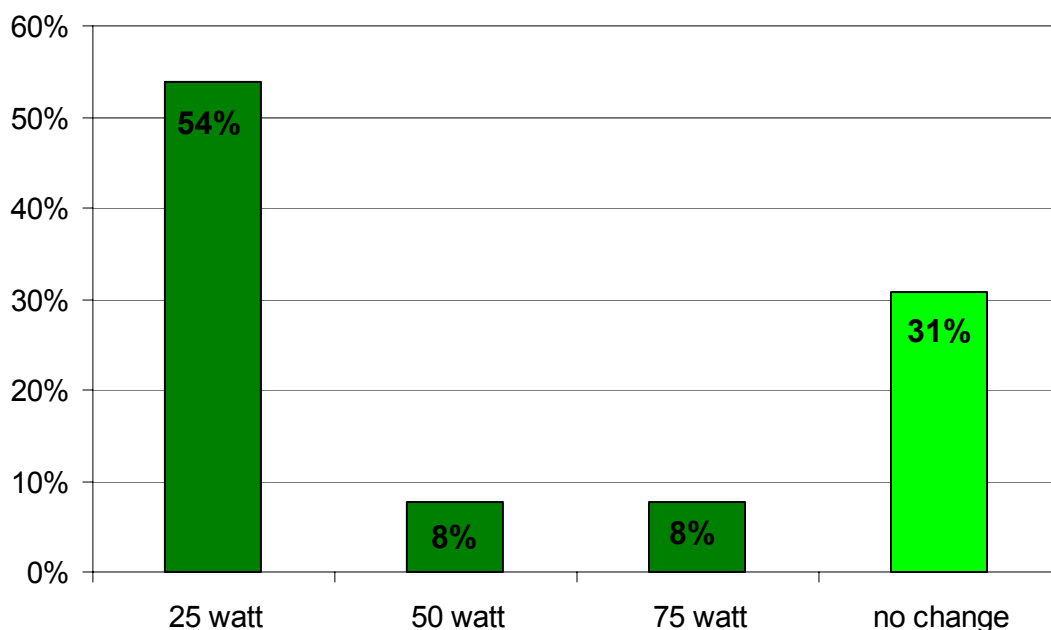


Figure C: The figure shows that 70% of patients have improved in at least 25 watt from baseline following NI-CATH. No patients have shown a decrease in exercise tolerance.

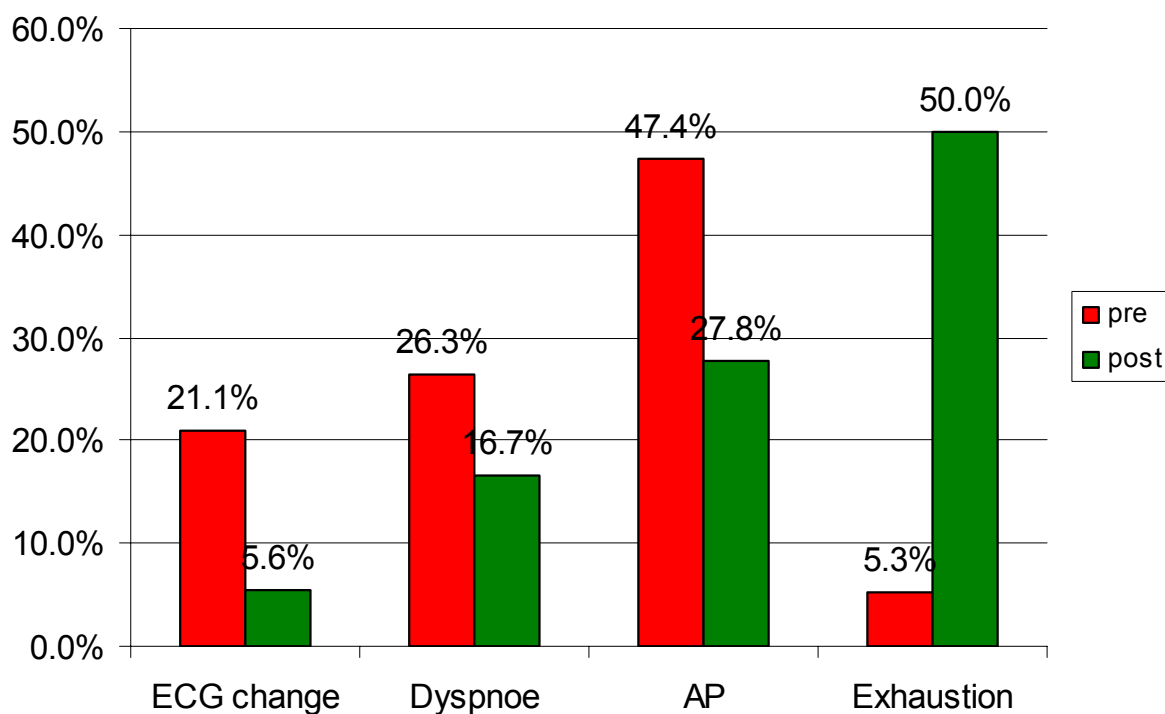


Figure D: The figure shows the percentage of patients who terminated the exercise test before and after NI-CATH treatment. After therapy, 50% of patients, compared to 95% before therapy, have terminated the exercise test prematurely.

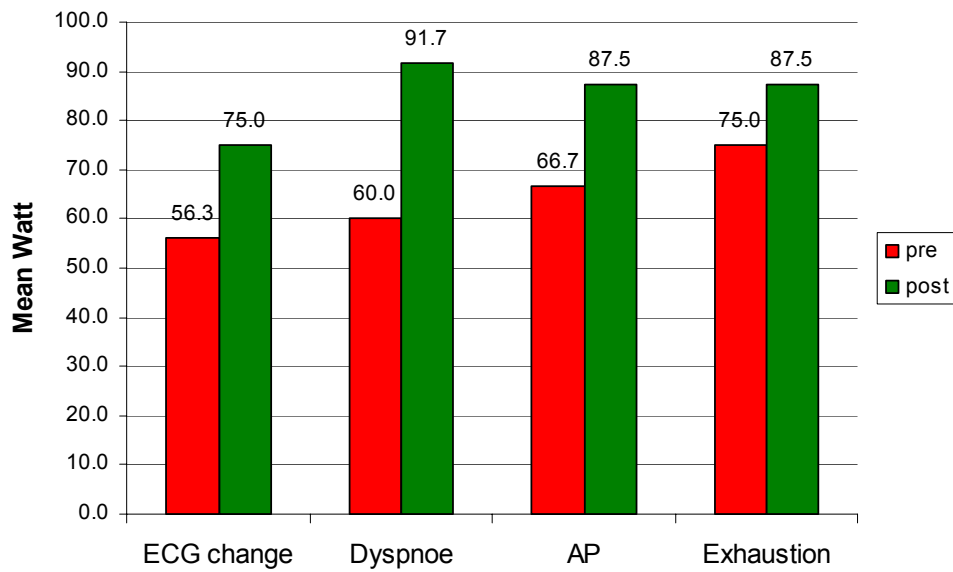


Fig E. The Exercise tolerance capacity of the patients who terminated the exercise test due to clinical symptoms has improved as well.

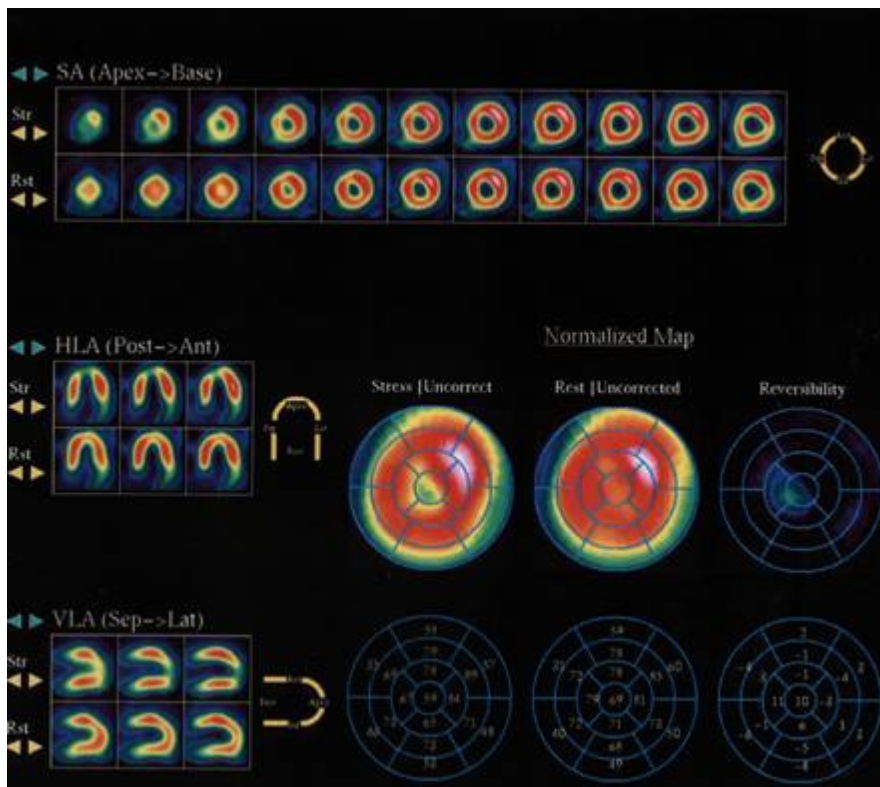


Fig F1. SPECT image of a typical patient before treatment. Reversible ischemia can be observed in the apical zone

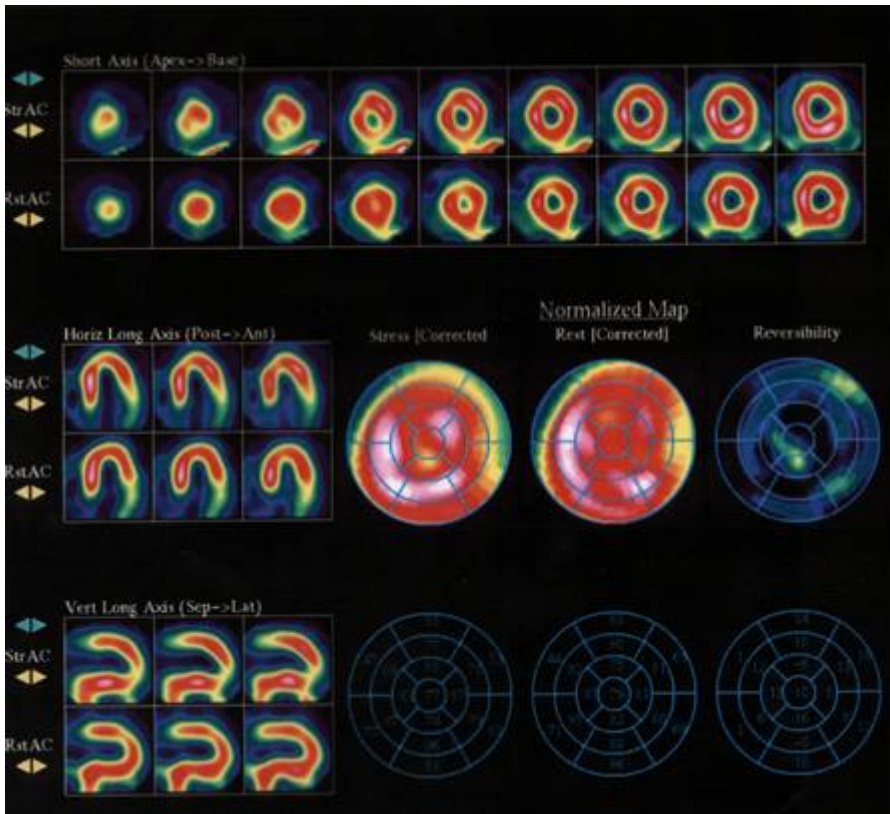


Fig F2. SPECT image of the same patient (Fig F1), 3 months post treatment. The Reversible ischemia that was observed in the apical zone was reduced significantly, resulting in improvement in angina symptoms.

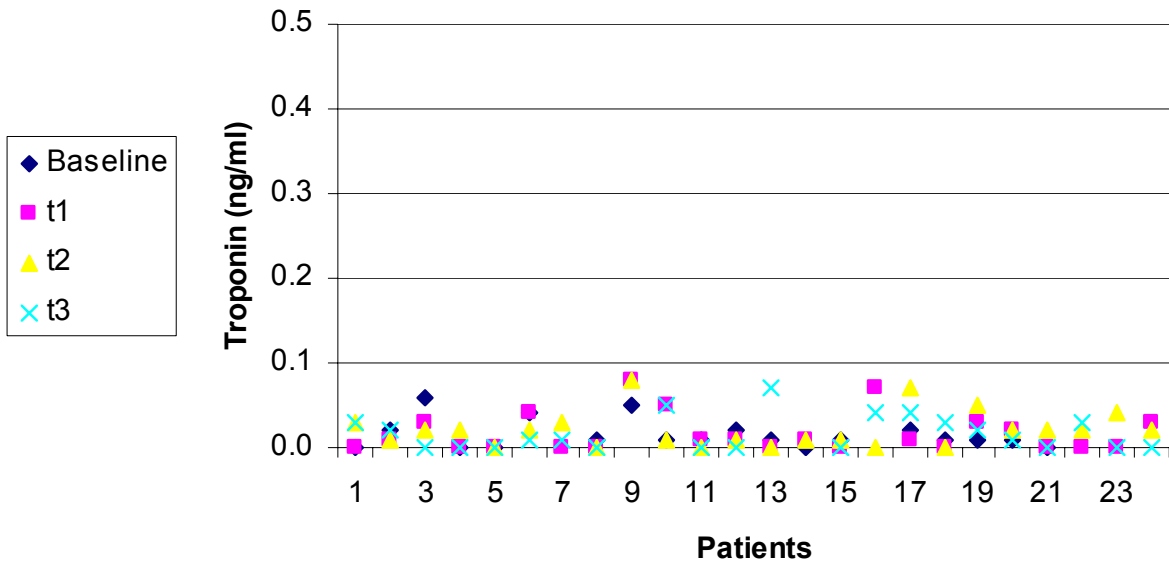


Figure G: Troponin level have not risen following each treatment (t1,t2,t3). Normal values are below 0.4 (ng/ml)