Method: We studied 15,579 consecutive patients (mean age 65±12, 41% females) who have been widely used in semiquantitative visual interpretation of myocardial perfusion SPECT [MPS] and has played important role in risk stratification. However, the prognostic value of MPS by an optimally weighted 17-segment scoring system has not been explored.

Results: We studied 15,579 consecutive patients (mean age 65±12, 41% females) who underwent exercise stress Tc-99m sestamibi MPS (n=15,579) and were followed up (96%) for 25±9.2 months (patients revascularized ≤50 days after MPS excluded). 17-segment scores were derived from 20-seg scores using an algorithm demonstrating excellent interobserver variability.

Conclusion: Noninvasive imaging of experimental induced atherosclerotic plaques by radiolabeled MCP-1 is feasible and might be useful for detection of the extent of inflammation in advanced atherosclerotic plaques and identification of plaques vulnerable to rupture.
Prolonged but Reversible Sarcolemmal Phosphatidyl Serine Expression in Myocardial Ischemia Represents Ischemic Memory and Can Be Noninvasively Detected by Radiolaabeled Annexin V Imaging

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Phosphatidyl serine (PS) is restrictively distributed to the inner leaflet of the sarcolemmal lipid bilayer in normal myocytes but gets externalized during apoptosis. Since apoptosis occurs commonly in ischemic stress and Annexin-V selectively targets externalized PS, we hypothesized that myocardial ischemia should be noninvasively detectable by radiolabeled imaging.

Severe myocardial ischemia was induced in 6 NZW rabbits by LAD coronary artery occlusion for 10 min followed by 30 min reperfusion. 99mTc-Annexin-V (~10mCi) was injected intravenously and animals were sacrificed at 3H. Ex vivo imaging demonstrated significant Annexin uptake in ischemic zone. Maximum percent injected dose per gram was 0.27+/-0.16 in ischemic compared to 0.03+/-0.01% in normal myocardium (ratio 9+/-4).

However, histopathologic and histochemical analysis did not reveal apoptosis or necrosis, and ultrastructural isolation of subcellular components of ischemic myocardium from cell membrane revealed that PS=0.5% of radioactivity had been internalized, possibly due to translocation of PS back to inner sarcolemmal leaflet upon reperfusion. To further characterize the reversibility of PS expression, we subjected mouse hearts to 5 min ischemia, and allowed reperfusion for 1.5, 3, 6, and 24H and injected Annexin-V 10 min before sacrifice. PS expression persisted for 6H. Internalization was traced to cytochalasin, mitochondria, and nucleus. These data indicate that persistent but reversible PS expression in ischemic myocardium offers an ischemic memory window for at least 6H. Noninvasive targeting of molecular alterations during severe ischemia, such as persistent PS expression, should lead to development of newer but spot imaging strategies, and after-the-fact recognition may provide novel means to differentiate cardiac from noncardiac origin of chest pain.

Positron Emission Tomography Imaging of Cardiac Cardiomyopathy

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Background: Cell transplantation is actively investigated as potential treatment for end-stage heart failure. However, traditional methods of determining engraftment rely on postmortem analysis. Development of an imaging technique to quantitatively localize and optimize transplant protocol would be beneficial. Methods: 1) Cell Culture: Rat cardiomyoblast cell line (H9C2) was transduced with Ad-CMV-HSV1-sr39tk to assess expression level of a P2 receptor gene (mutant viral thymidine kinase (vTK)). In Vitro Transfected myoblasts (3x10^6) were injected into anterolateral wall of nude rats (n=5) via thoracotomy. Control rats (n=3) received myoblasts expressing firefly luciferase. MicroPET imaging on living rats was performed on days 2 and 5 using tracer (Sodium [3^2P]thymidine kinase (vTK)). Results: 1) Transfected myoblasts yield radiolabel sr39tk activity: 3x10^6 myoblasts (4.42x1.79), 2x10^6 (3.92x1.26), and 1x10^6 (1.86x0.28% conversion/ug protein/min) versus control (0.02x0.01). 2) MicroPET imaging show 19% of injected myoblasts at anterolateral wall on day 2 (0.046x0.008) and day 5 (0.038x0.013%ID/Bg) versus control (0.019x0.012%ID/Bg). Immunohistochemistry and autoradiography confirm presence of transplanted myoblasts. Conclusion: This is the first proof-of-concept study on noninvasive PET imaging of cardiac cell transplantation. Further validation and refinement of the approach described may lead to wider research and clinical application.