THE SOCIETY OF THORACIC SURGEONS
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Testimony on behalf of
THE SOCIETY OF THORACIC SURGEONS

Presented by

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President, STS, January, 2003 – January, 2004
Professor and Chief of Cardiothoracic Surgery
Emory University School of Medicine, Atlanta, GA

to the

MEDICARE COVERAGE ADVISORY COMMITTEE

July 14, 2004

Disclosure

- Consulting relationship with Medtronic and Quest Medical. To my knowledge, these device companies have no activity in TMR.
- From Cardiogenesis - investigational research support (animal studies) in our laboratory involving other Emory investigators (not myself).
- No other relationship to Edwards or Cardiogenesis.
- My travel expenses for this testimony are paid by The Society of Thoracic Surgeons.

Other Qualifications

- STS leadership role – as Treasurer then President – member of the Executive Committee for the last nine years.
- Active clinical surgeon – approximately 350 operations per year for 24 years.
- Active educator – Director of Emory's Thoracic Surgery Residency program – 70 thoracic surgeons trained during my faculty tenure.
- Co-chairperson of the ACC-AHA committee on Guidelines for Coronary Artery Bypass, 1997 to present.

The STS and Innovation

- Mission – Help Cardiothoracic Surgeons Serve Patients Better.
- We will work to develop, to refine, and to bring to clinical practice advances in
  - molecular biology,
  - pharmacology,
  - information technology for facilitating and improving clinical practice,
  - operative techniques,
  - surgical devices.

The Challenge of Innovation

- # 1 Priority – Remain Patient-Centered
  - Evaluate and re-evaluate new technology.
  - Maintain constant focus on patient benefit.

STS and New Technology
Evaluation and Focus on Patient Benefit

- **<u>STS Workforce on New Technology</u>**
  - **Video-thoracoscopy for intrathoracic disease**
  - **Minimally invasive coronary bypass**
  - **Left Ventricular Remodeling for CHF (Batista)**
  - **Left ventricular assist devices for destination therapy**
  - **Lung volume reduction surgery**
- **<u>STS Workforce on Evidence-Based Medicine</u>**
  - **Guideline on Transmyocardial Revascularization**

STS and New Technology
Evaluation and Focus on Patient Benefit

- **STS Adult Cardiac Database**
  - **20 years experience, 2/3 of U.S. centers.**
  - **Accurate information regarding patient characteristics and outcomes allow for continuing improvement and refinements in patient selection, surgical technique, post-op management, and practitioner education**
  - **AHRQ Grant to proactively use data management to improve clinical processes.**
  - **Platform for prospective RCT's.**
  - **Observational evaluation of TMR**

STS and TMR

Evaluation and Focus on Patient Benefit

Comment on MCAC Questions

- TMR alone
  - strongly supported by RCT's and observational studies
- TMR + CABG
  - Less data, more difficult to interpret
- PMR – No comment from STS
- Confounding factors important in these deliberations

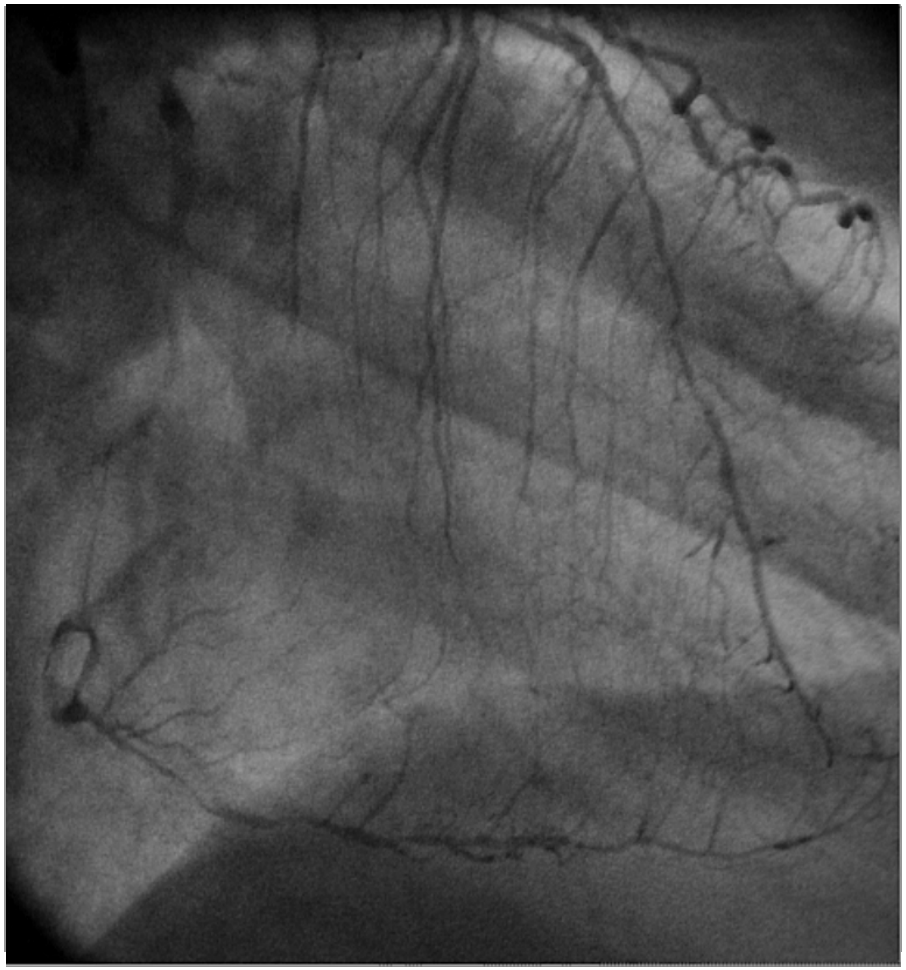
Begin with Patient Perspective Who are these patients?

- Patients with DIFFUSE CORONARY DISEASE not amenable to PCI/CABG Rx.
  - Up to 12% of patients with CAD[1]
  - Cause of Incomplete Revascularization in 15 to 25% of CABG patients[2]

[1]Muhkerjee D, et al. Am J Cardiol 1999;84:598-600.

[2]Weintraub W, et al. Am J Cardiol 1994;73:103-12.

Long Term Risk of Diffuse CAD



Incomplete revascularization due to small or diffusely diseased vessels significantly increases the risk of late cardiac events

Lawrie G, et al. Circulation 1982;66:717-23.
Bell MR, et al. Circulation 1992;86:446-57.
Schaff H, et al. Circulation 1983;68:II200-04.

TMR: *Treatment of Patients Afflicted by Diffuse CAD*

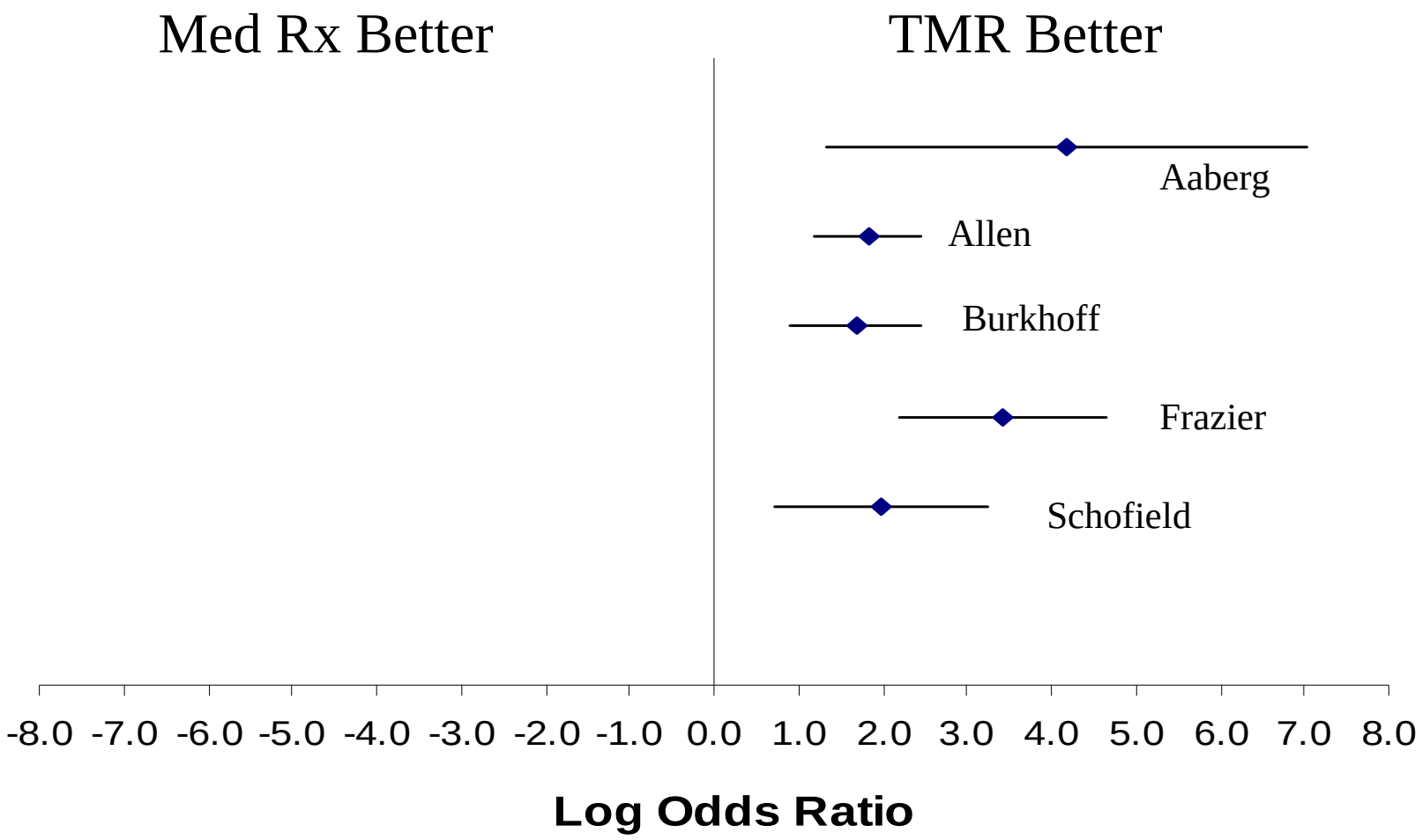
- **1981 Report of animal trials of Laser TMR**
- **1990 Clinical Studies begun in U.S.**
- **1997-2000**
  - **Reporting of 5 RCTs with One Year Follow-up**
    - TMR as sole therapy (5) and TMR/CABG (2)
- **1998-1999**
  - **FDA approvals for 2 TMR devices**
  - **Medicare reimbursement: sole and adjunctive therapy**
- **2002-2004**
  - **Reporting of long-term follow-up of 3 RCTs**
  - **Observational study of TMR usage from STS Database**

TMR As Sole Therapy for Disabling Angina

937 Randomized Patients in 5 Controlled Trials

- **Early (≤30 days) mortality**
  - Stable angina patients: 1% to 5%
  - Unstable angina patients: 9% to 22%
- **One year outcomes**
  - Survival equal to medical management
  - Morbidity equal to medical management
  - IMPROVED prospectively defined event-free survival
  - IMPROVED quality of life
  - Dramatically IMPROVED angina class

5 RCTs - Reduction in Angina ≥ 2 Classes

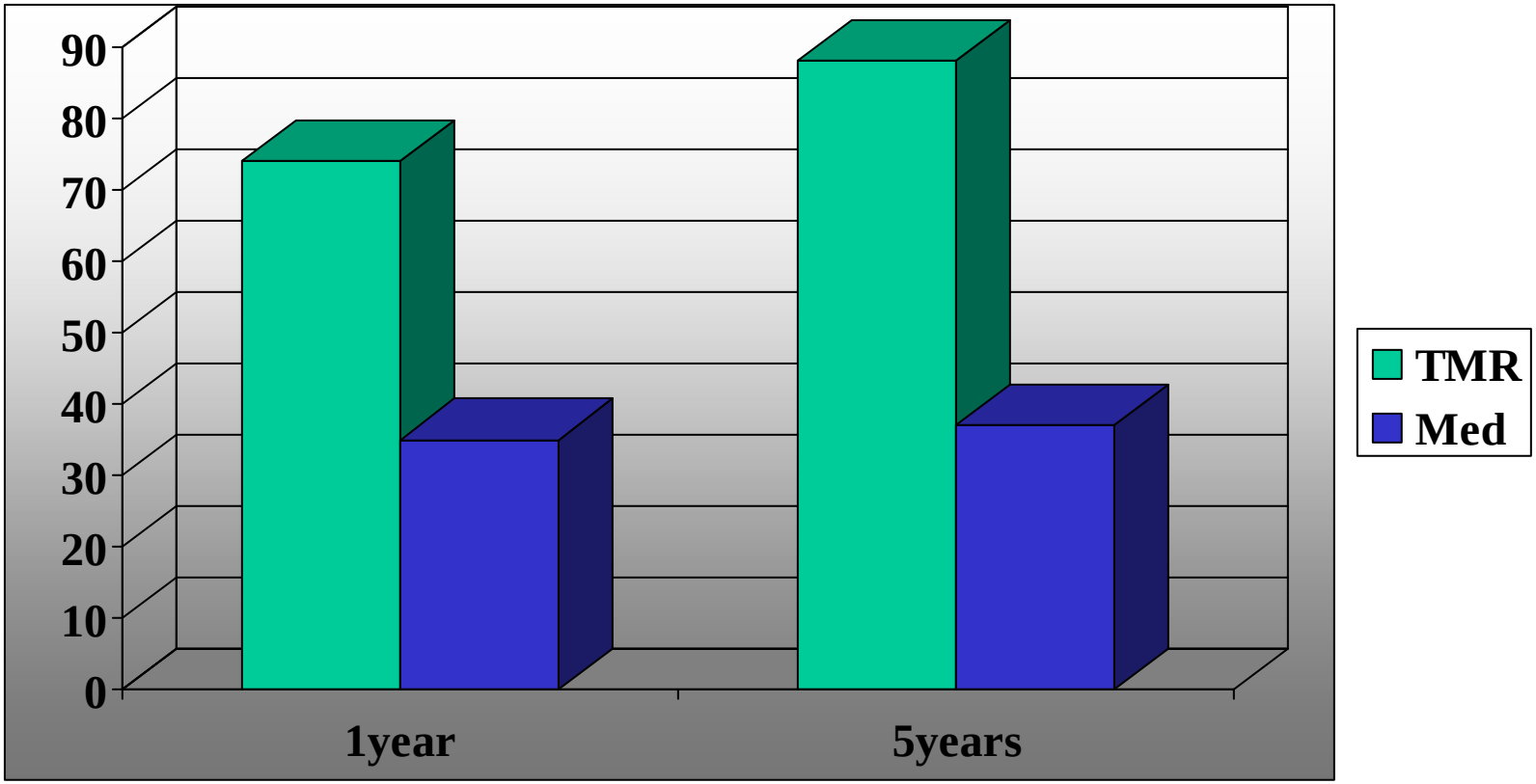


Source: ECRI Technology Assessment, 2003

TMR vs Med Rx RCT (Allen)

Sustained benefit at five years

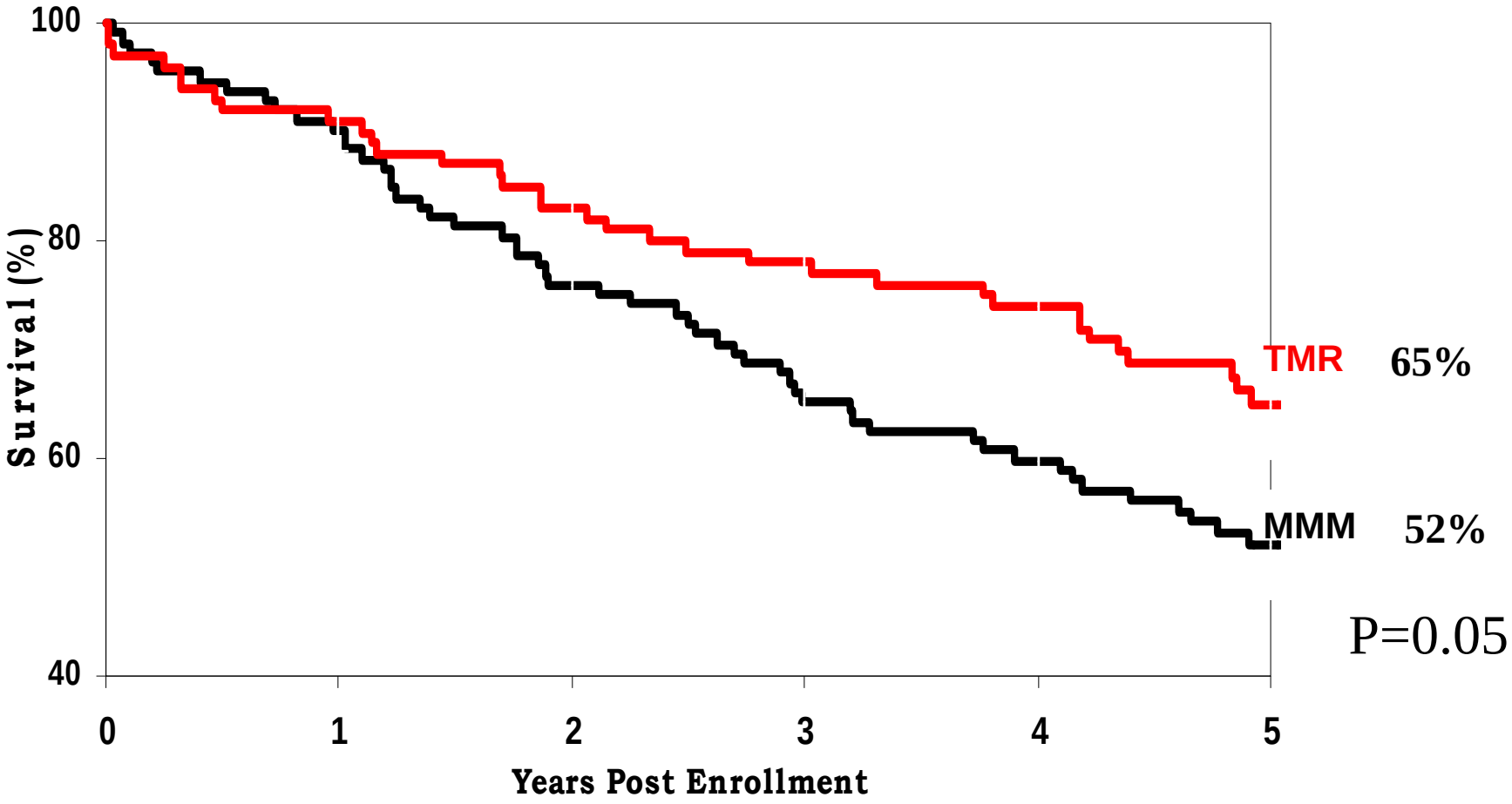
% freedom from Class III or IV angina



Five-Year Kaplan-Meier Survival

Intent-To-Treat Analysis

Allen KB, et al. Ann Thorac Surg 2004;77:1228-34.



From the Patient's perspective:

For the patient disabled with Class IV angina with Diffuse CAD not amenable to PTI/CABG, TMR vs Medical management:

- *At one year: DRAMATIC symptom improvement (3/4 chance of freedom from disabling angina) with minimal downside: NO difference in 1 year mortality or morbidity.*
- *At five years: <u>SUSTAINED symptom improvement</u> (88% chance of freedom from disabling angina at five years) AND 27% relative five year <u>mortality benefit</u> with TMR.*

Adjunctive TMR - a more difficult issue

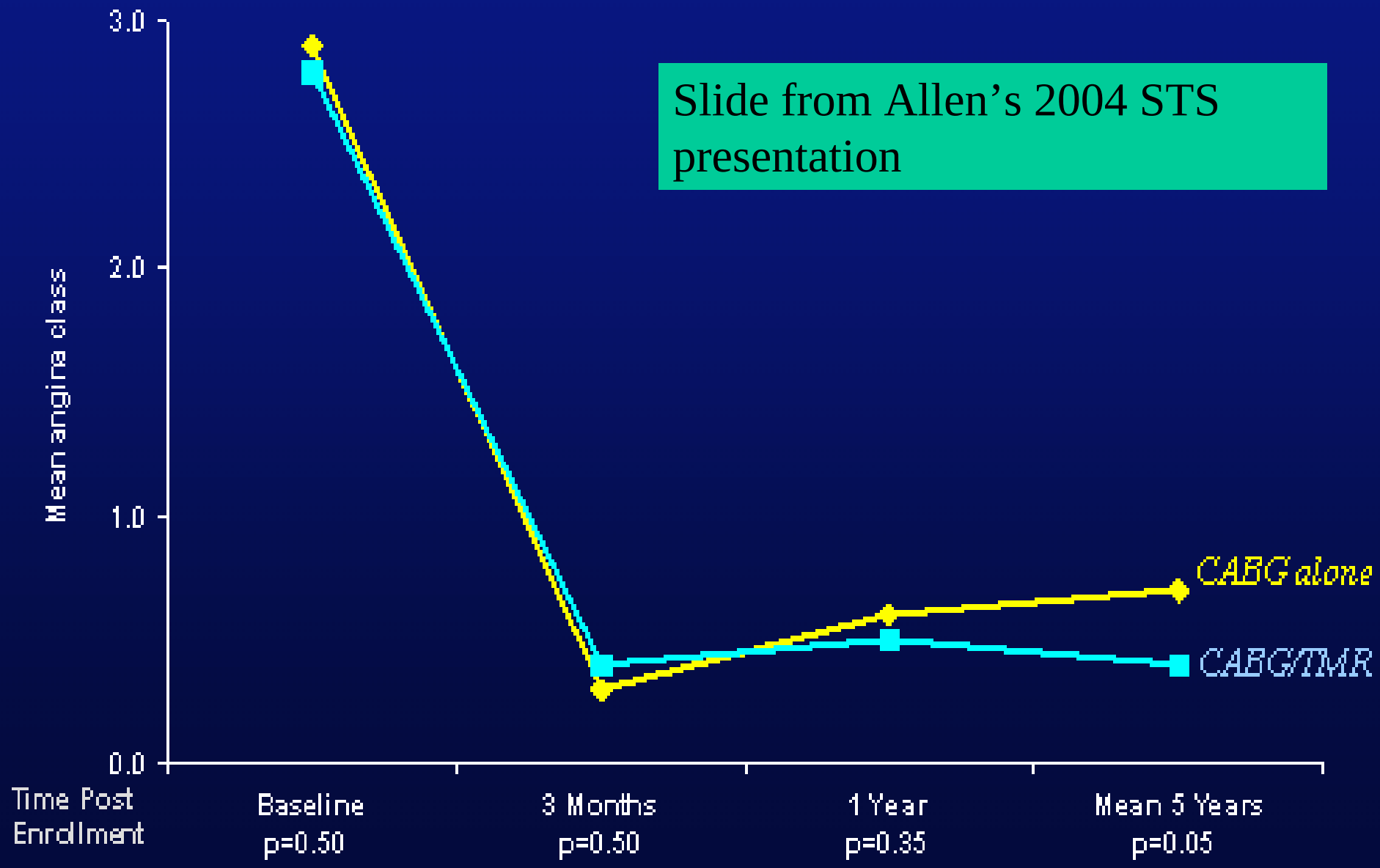
- Data is not “clean” – variables cannot be isolated:
- TMR is being added to a therapy directed at the same symptom – because potential benefit is incremental, one would expect many more patients would be needed to show benefit.
- Control group cannot be created by case-matching or propensity score analysis because diffuse coronary disease is very difficult to quantify (or even identify) in databases, probably has a very negative impact on long-term outcomes, and is present in all TMR patients and only ~20% of CABG patients.

Adjunctive TMR - ? Incremental benefit ?

- What data do we have?
- Two RCTs, only one of reasonable size (Allen et al.):
  - 263 patients at 24 U.S. centers
  - Five year follow-up
- Observational data from STS Database (Peterson et al.)-

Long-Term Mean Angina Class

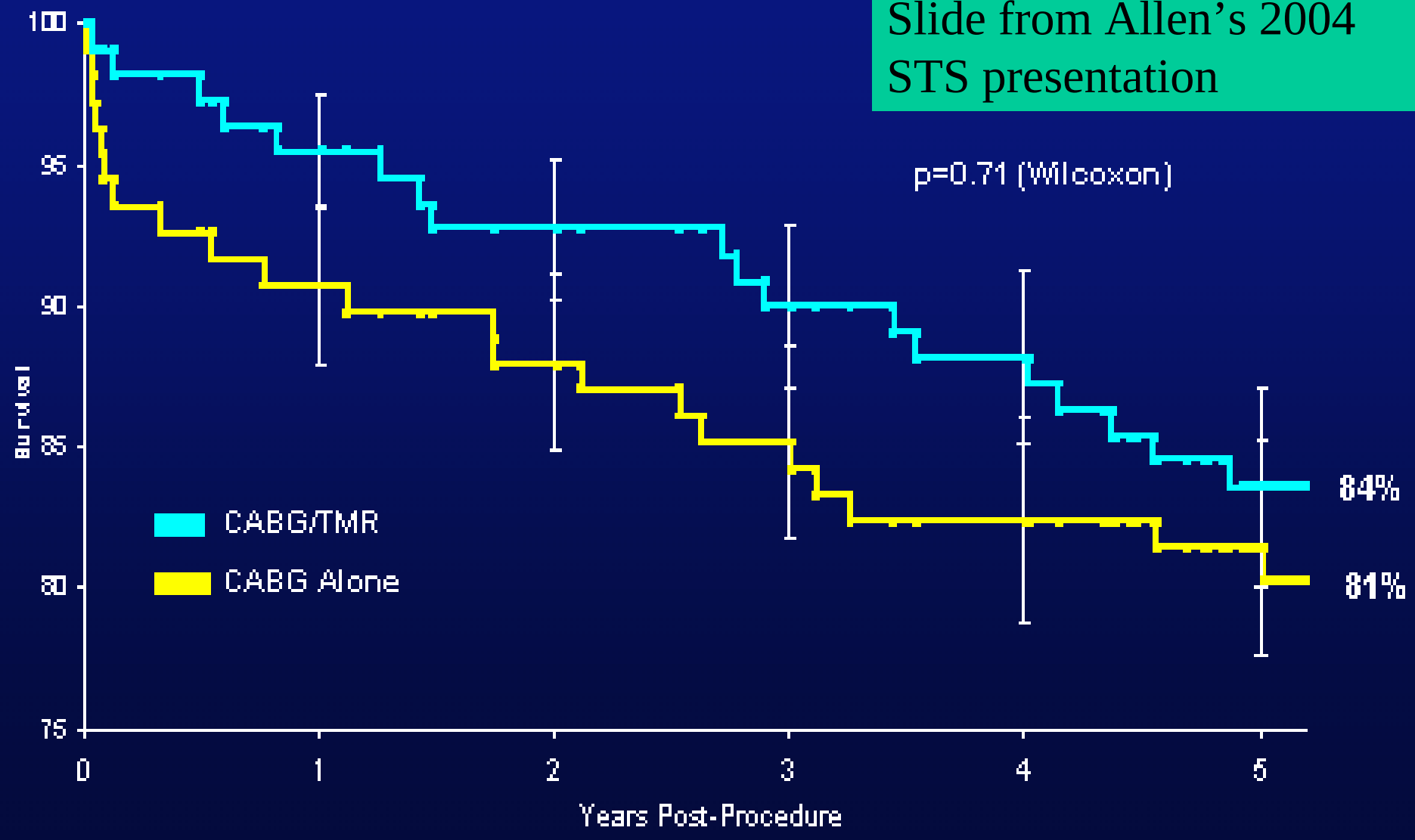
Randomized Patients



Slide from Allen's 2004 STS presentation

Five-Year Kaplan-Meier Survival

Slide from Allen's 2004 STS presentation



Adjunctive TMR - ? Incremental benefit ?

- RCT showed thirty day and one year survival benefit – however, the observational study failed to confirm the thirty day survival benefit.
- RCT showed a statistically significant five year benefit in angina class.
- Peterson's observational study confirmed the *absence* of a "downside" of adding TMR to CABG: mortality and morbidity were not increased.

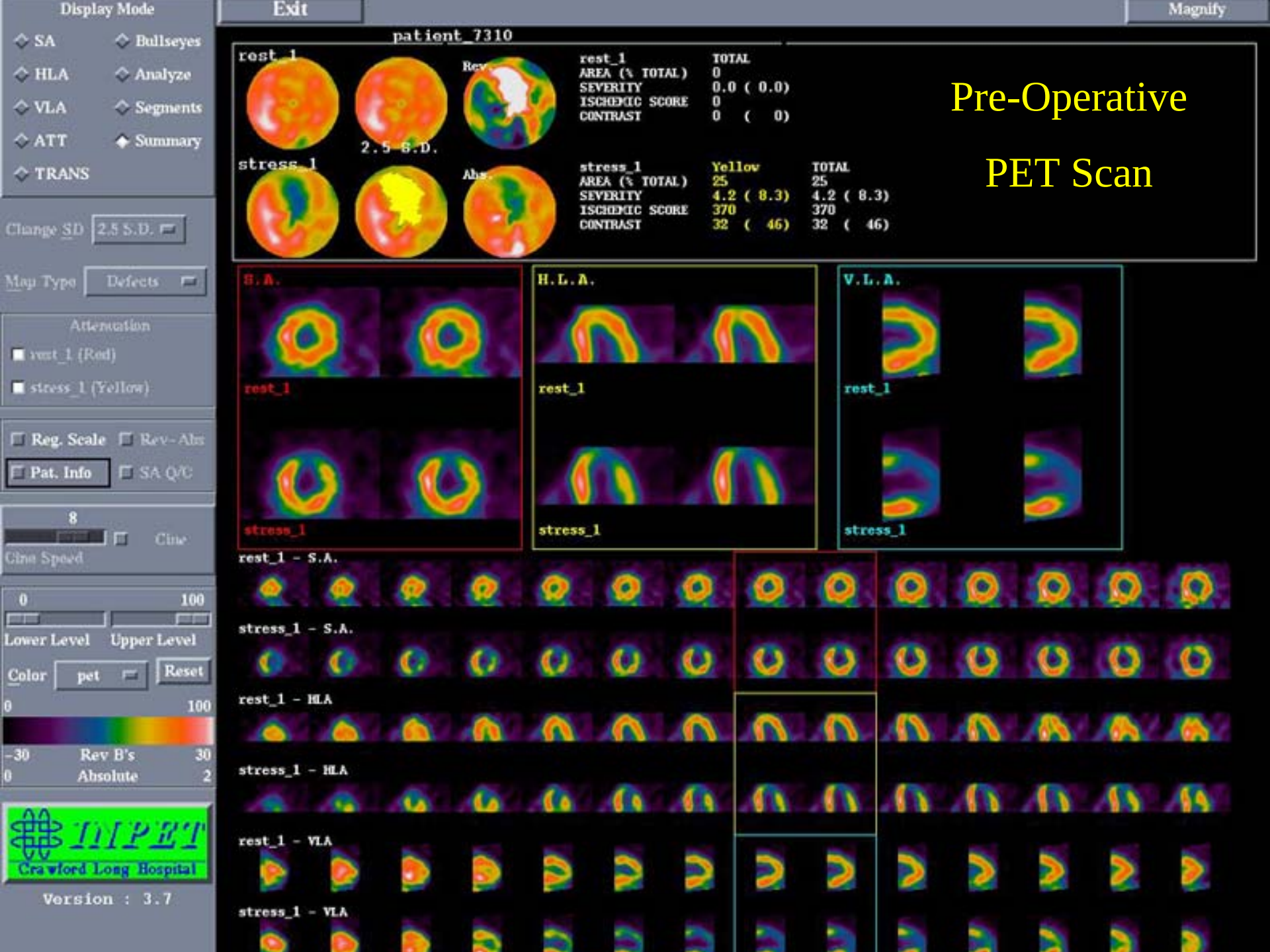
From the Patient's perspective:

A patient disabled with angina scheduled to undergo CABG but with a large region of diffuse CAD likely not amenable to CABG

- RISK/BENEFITS/ALTERNATIVES
- Incremental risk – essentially none.
- Incremental benefit – possible early survival benefit, probable late benefit in angina relief.
- Alternative – Incomplete revascularization with CABG alone – known to be associated with increased operative and long-term risk compared to complete revascularization.

From the perspective of a clinical cardiac surgeon:

- Resisted TMR for years
- If ever there was a physician wedded to system physiology, it is Robert Guyton
- “Come talk to me again when you have five year data.”
- Local clinical observations…


Pre-Operative
PET Scan
Display Mode
SA
Bullseyes
HLA
Analyze
VLA
Segments
ATT
Summary
TRANS
Exit
Magnify
patient_7310
rest_1
2.5 S.D.
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SA Q/C
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Cine Speed
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Upper Level
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Reset
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100
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rest_1
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stress_1 - HLA
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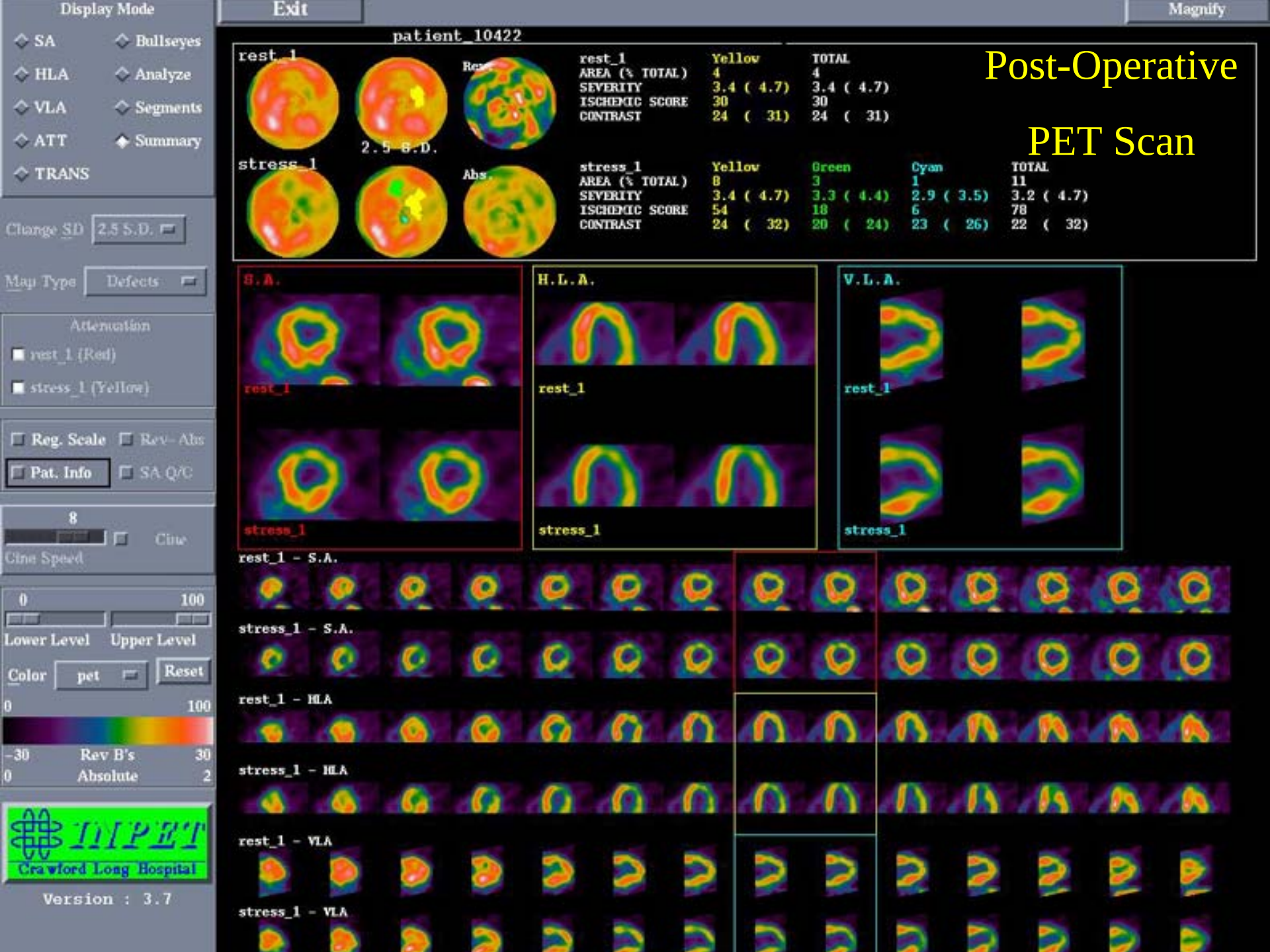
stress_1 - VLA

Post-Operative

PET Scan



Carlyle Fraser Heart Center Retrospective TMR Study

- 10 pts with TMR as sole Rx had preop PET scans
- 7 of 10 returned for repeat scan
- Perfusion improvement seen in 6 of 7
- The patient without clinical improvement was the one without perfusion improvement

Carlyle Fraser Heart Center Retrospective TMR Study

- Change in size alone of ischemic defects not significant. 30%/L.V. vs 23.6%/L.V. *(p - N.S.)*
- Significant decrease in size/severity of ischemic defects. 131 vs 88.2 *(p<.05)*
- A small, but significant increase was seen in LV scar (2% of LV, p<0.05)

From the perspective of a clinical cardiac surgeon:

- Resisted TMR for years
- If ever there was a physician wedded to system physiology, it is Robert Guyton
- “Come talk to me again when you have five year data.”
- Local clinical observations…

Confounding Issue

- **“UNSTABLE ANGINA”** – as defined in most of the RCTs of TMR is an extreme interpretation – Angina *requiring* intravenous antianginal Rx, IABP and/or heparin.
- Although TMR in this setting has a high risk, the therapeutic options are indeed limited in patients with diffuse CAD who are unweanable from intravenous medications.

Confounding Issue

- The pejorative term **"off-label use"** as applied without qualification in the Peterson paper to TMR + CABG is problematic for me.
- At the time of FDA approval of TMR devices (1998, 1999) this issue was raised at the Panel discussion and resulted in the careful wording used in the approval statement and approved indication for use.
- HCFA (CMS) further issued, in October 1999, a coverage policy addendum stating that CABG + TMR was a covered use of TMR if "the laser is being used in accordance with its FDA approval for use…" which clearly implied that in selected cases CABG + TMR was in accordance with the FDA approval.

Confounding Issue

- Peterson reported a finding of **"widespread use of TMR+CABG"** and expressed some concern at the rapid growth of the procedure from 1998 thru 2001.
- This is exactly the period in which the RCT of TMR+CABG reported a significant one year survival benefit.
- The usage at the end of the study period was found in 36% of STS cardiac sites and the median TMR usage in these sites was 12 per year. A usage of once per month in one-third of the centers is considerably less than my threshold for application of the term "widespread use".

Summary

- TMR as sole therapy for disabling angina (both stable and unstable) has a low risk and a great benefit, established by multiple RCT's and observational studies.
- TMR+CABG for disabling angina with an area of myocardium not amenable to PTI/CABG has no incremental risk compared to CABG alone. It has a very likely incremental benefit in long term symptom relief in selected patients.
- CMS coverage needs to continue - TMR addresses an otherwise unmet need in a seriously ill patient subset.

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