INCAPS – implications for Nuclear Cardiology
IAEA Nuclear Cardiology Protocol Study

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QUANTA, Curitiba – Brazil
Consultant IAEA, Austria
Chairman International AP, ASNC, USA
risk of testing vs risk of not testing

Harmful ?

Useful ?
Topics to cover
risk of testing vs risk of not testing

- The epidemics of CVD
  - The growing problem of CVD mortality in developing countries
  - Are developing countries investing enough to decrease mortality ?
  - Is imaging used enough in developing compared to developed countries ?

- The patient being tested and the nuclear technique applied
  - Do I know my patient clinical history ? Did I plan the best work up strategy ?
  - Patient Centered Imaging
  - Justification - Is Appropriate to test this patient using Nuclear ? – AUC
  - Optimization – protocol used ? Am I testing correctly to minimize radiation exposure ?
  - Am I complying with the ALARA principle in my lab ?

- The future
  - INCAPS show us opportunities for improving NC practice worldwide ~ ALARA
Clinical Case - from Curitiba - Brazil

risk of testing vs risk of not testing

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51 yo Man, HTN, obese
DM, Fam Hx CAD
NO HISTORY OF CAD

Atypical chest pain, referred for outpatient MIBI
Clinical Cases from Curitiba - Brazil

risk of testing vs risk of not testing

51 yo Man, HTN, obese DM, Fam Hx CAD NO HISTORY OF CAD

Atypical chest pain, referred for outpatient
57 yo male, recent onset chest pain, MPI ordered. Injected activities were weight-based. 8 minutes, on the Bruce protocol. Heart rate from 65 to 157 bpm. BP 120/80 to 190/100 mmHg. Patient had chest pain near peak exercise (non-limiting), 1 mm ST depression.
Risk Based on Exercise Testing?

DUKE TREADMILL SCORE

- Calculation: + mins - 5 x ST - 4 x angina

<table>
<thead>
<tr>
<th>Risk</th>
<th>Score</th>
<th>Mortality/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>≥ 5</td>
<td>0.25%</td>
</tr>
<tr>
<td>Interm</td>
<td>4.... -10</td>
<td>1.25%</td>
</tr>
<tr>
<td>High</td>
<td>≤ -11</td>
<td>5.25%</td>
</tr>
</tbody>
</table>

• Nuclear rarely
• Nuclear for most
• Nuclear for some
### Risk Based on Exercise Testing?

**DUKE TREADMILL SCORE**

**Calculation**: 
\[ +8 - 5 \times 1 - 4 \times 1 : -1 \]

<table>
<thead>
<tr>
<th>Risk</th>
<th>Score</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>( \geq 5 )</td>
<td>0.25% • Nuclear rarely</td>
</tr>
<tr>
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<td>4.... -10</td>
<td>1.25% • Nuclear for most</td>
</tr>
<tr>
<td>High</td>
<td>( \leq -11 )</td>
<td>5.25% • Nuclear for some</td>
</tr>
</tbody>
</table>
risk of testing vs risk of not testing

Figure 4
A 59 yo man, diabetic, hypertensive, dyslipidemic, smoker with atypical symptoms

**risk of testing vs risk of not testing**
risk of testing vs risk of not testing
Fig. 6 SPECT-MPI of a 75-year-old woman presenting with shortness of breath and no chest pain. Observe the large moderate to severe defect, mostly reversible defect (ischemia), involving the infero-septal, septal, and apical regions of the heart. There is also evidence of transient ischemic dilation. These are high-risk markers for death. This patient had sudden death at home within days following this study.
Perfusion Patterns Predict Events

A

Log-rank p-value < 0.001
Event Rate: 13.1% (72/548)

Adjusted All-cause Mortality Incidence (%)

Event Rate: 4.0% (67/1677)

Number at Risk
Normal SPECT
1677
1638
1611
1358
784
Abnormal SPECT
548
413
372
307
172

B

Log-rank p-value < 0.001

Adjusted All-cause Mortality Incidence (%)

Normal
1677
1638
1611
1358
784
Mild/Mod Reversible
382
302
278
228
128
Fixed
53
43
39
35
20
Partial Reversible
52
35
30
28
17
Severe Reversible
61
36
28
19
11

JACC img, August 2011
The growing problem of CVD mortality in developing countries
80% of the deaths due to CVD

Severe ischemia > 10% of LV

Post 1 stent LAD

High Risk

Can we lower the risk by revascularization beyond OMT?
(Ischemia trial …)

Habibian R, Delbeke D, Martin W, Sandler M, Vitola JV
Cardiovascular Imaging, in Nuclear Medicine Teaching File, 2009
• The growing problem of CVD mortality in developing countries
Investing in healthcare (prevention + diagnosis + treatment) how do we know investment works?

**Figure 69** Trends in CVD mortality rates (age standardized) in developed countries (\(x_i\)).

Source: WHO
Investing in healthcare (prevention + diagnosis + treatment) how do we know investment works?

US decline in heart disease mortality
Are developing countries investing enough to reduce mortality?

Is imaging (nuclear) used enough in developing countries?

How much of the reduction in mortality observed in developed nations has to do with imaging (nuclear)?

How much imaging (nuclear) is being done where mortality is lower and higher worldwide?
Underutilized or non existent in Many Nations ~ where mortality is high!
Worldwide CVD mortality vs Use of Cardiac Imaging

Influenced by:
- Economy
  GDP
  Healthcare Policies
- Information
  Organized scientific groups
  Local Scientific Production
  Training
- Neighboring countries
  Communication
  Training
  Scientific meetings

Vitola JV, Shaw L, Allam A et al. JNC 2009
Tendencies Advanced Cardiac Imaging Regionally in Curitiba, Brazil

Figure 2. Number of studies performed per year in 2 referral centers (Quanta and DAPI) in Curitiba, Brazil. Population of 1.7 million inhabitants. Source: Quanta Registry, Vitola JV, Cerci R, Zapparoli M. SPECT, single photon emission computed tomography; CCTA, computed coronary tomography angiography; CMR, cardiac magnetic resonance.

procedures at two referral centers for non-invasive cardiac imaging in a city of 1.7 million inhabitants in Latin America (Curitiba, Brazil), demonstrating pro-
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IAEA Nuclear Cardiology Protocol Study

risk of testing vs risk of not testing

Harmful ?

Useful ?

Justification
Optimization
ALARA
INCAPS Background

- 15-20 million myocardial perfusion imaging (MPI) studies performed per year worldwide (most North America)
- High radiation doses have been described
- Low radiation doses have been described
- Single-country data (e.g. US and Germany) suggests that radiation safety technique is frequently suboptimal
- No previous study characterized nuclear cardiology practices impacting radiation globally
- A needs assessment expert meeting was organized by IAEA in 2012 and identified knowledge of worldwide MPI protocols, practices, and dosimetry as an important priority

INCAPS
IAEA Nuclear Cardiology Protocol Study

- International cross-sectional study of nuclear cardiology utilization, dosimetry, and protocols
- Executive committee, Regional coordinators around the globe, Investigators group members from 65 countries
- Performed with assistance of many professional societies

Current worldwide nuclear cardiology practices and radiation exposure: results from the 65 country IAEA Nuclear Cardiology Protocols Cross-Sectional Study (INCAPS)

Andrew J. Einstein¹,²*, Thomas N. B. Pascual³, Mathew Mercuri¹, Ganesan Karthikeyan⁴, João V. Vitola⁵, John J. Mahmarian⁶, Nathan Better⁷, Salah E. Bouyoucef⁸, Henry Hee-Seung Bom⁹, Vikram Lele¹⁰, V. Peter C. Magbooh¹¹,¹², Erick Alexánderson¹³, Adel H. Allam¹⁴, Mouaz H. Al-Mallah¹⁵, Albert Flotats¹⁶, Scott Jerome¹⁷,¹⁸, Philipp A. Kaufmann¹⁹, Osnat Luxenburg²⁰,²¹, Leslee J. Shaw²², S. Richard Underwood²³,²⁴, Madan M. Rehani²⁵, Ravi Kashyap³, Diana Paez³, and Maurizio Dondi³, for the INCAPS Investigators Group
INCAPS Methodology

• On March 15, 2013, IAEA contacted potential sites and requested they participate voluntarily

• Labs asked to provide all data on studies completed in a selected week March 19-April 22, 2013

• Standardized data collection instrument collected data on
  – Lab demographics
  – Patient demographics and clinical characteristics for each MPI study completed during selected week
    • Age, gender, weight, radiopharmaceuticals and activities, camera type, patient positioning, hardware and software

INCAPS Methodology

• Radiation exposure quantified using effective dose (ED), determined using standard ICRP methodology
  – Median lab ED ≤ 9 mSv, as specified by ASNC guidelines, evaluated for each lab
• Eight radiation-related “best practices” identified by IAEA expert panel prior to analysis
• A lab quality index (QI) determined as the number of best practices used (0-8) during the week
  – QI score of 6 or greater prespecified as desirable level
• Hierarchical regression model studied relationship between best practice adherence and predicted patient ED
  – Dependent variable: patient ED
  – Independent variables: 8 best practices, patient age, gender, weight

8 Best Practices

- **Avoid TI-201 stress**: No TI-201 stress tests were performed in patients ≤70 years.
- **Avoid dual isotope**: No dual isotope (rest TI-201 and stress Tc-99m) studies were performed in patients ≤70 years (both excluding viability).
- **Avoid too much Tc-99m**: No study w. Tc-99m activities >1332 MBq (36 mCi), and mean total effective dose was <15 mSv for all studies with two Tc-99m injections.
- **Avoid too much TI-201**: For each study with TI-201, <129.5 MBq (3.5 mCi) at stress.
- **Perform stress-only imaging**: Lab performed 1+ stress-only study, in which rest imaging was omitted, or the laboratory did only PET-based stress tests.
- **Use camera-based dose-reduction strategies**: Lab performed at least one study using at least one of the following: 1) attenuation correction, 2) imaging patients in multiple positions, e.g. supine and prone, 3) high-technology software (e.g. resolution recovery), and 4) high-technology hardware (e.g. PET or CZT).
- **Weight-based dosing for Tc-99m**: The laboratory had a positive correlation between patient weight and administered activity (MBq), for injections of Tc-99m.
- **Avoid inappropriate dosing that can lead to "shine-through" artifact**: Lab performed no SPECT studies with Tc-99m rest and stress injections on same day, in which the activity of the second injection was less than 3 times that of the first injection.
## Radiation Effective Doses by Patient

<table>
<thead>
<tr>
<th>Region</th>
<th>Africa</th>
<th>Asia</th>
<th>Europe</th>
<th>Latin America</th>
<th>North America</th>
<th>Oceania</th>
<th>World</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>9.7</td>
<td>11.4</td>
<td>7.9</td>
<td>11.8</td>
<td>10.5</td>
<td>9.3</td>
<td>10.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IQR</td>
<td>5.1-15.6</td>
<td>9.2-13.5</td>
<td>5.1-10.1</td>
<td>8.4-14.6</td>
<td>8.0-12.9</td>
<td>6.5-11.7</td>
<td>6.7-12.7</td>
<td>n/a</td>
</tr>
<tr>
<td>Range</td>
<td>1.8-20.0</td>
<td>1.0-35.6</td>
<td>0.8-25.9</td>
<td>2.2-27.1</td>
<td>0.9-28.1</td>
<td>0.9-17.9</td>
<td>0.8-35.6</td>
<td>n/a</td>
</tr>
<tr>
<td># with ED≤9mSv</td>
<td>173(50%)</td>
<td>358(24%)</td>
<td>1420(60%)</td>
<td>304(27%)</td>
<td>649(30%)</td>
<td>161(37%)</td>
<td>3065(39%)</td>
<td>&lt;0.001</td>
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</tbody>
</table>

(ASNC recommendation < 9 mSv)
<table>
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<td>8.4-14.6</td>
<td>8.0-12.9</td>
<td>6.5-11.7</td>
<td>6.7-12.7</td>
<td>n/a</td>
</tr>
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</tr>
</tbody>
</table>
Table 2. Latin America laboratory volume, radiation dose, and quality index score

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Patients</th>
<th>$\text{ED (mSv)}$</th>
<th>QI score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Argentina 1</td>
<td>67</td>
<td>10.1</td>
<td>0.80</td>
</tr>
<tr>
<td>Argentina 2</td>
<td>6</td>
<td>13.8</td>
<td>2.53</td>
</tr>
<tr>
<td>Argentina 3</td>
<td>62</td>
<td>9.6</td>
<td>4.95</td>
</tr>
<tr>
<td>Argentina 4</td>
<td>10</td>
<td>12.6</td>
<td>1.65</td>
</tr>
<tr>
<td>Argentina 5</td>
<td>76</td>
<td>12.8</td>
<td>3.48</td>
</tr>
<tr>
<td>Brazil 1</td>
<td>173</td>
<td>8.9</td>
<td>3.72</td>
</tr>
<tr>
<td>Brazil 2</td>
<td>23</td>
<td>12.0</td>
<td>2.94</td>
</tr>
<tr>
<td>Brazil 3</td>
<td>7</td>
<td>17.8</td>
<td>2.00</td>
</tr>
<tr>
<td>Brazil 4</td>
<td>24</td>
<td>12.2</td>
<td>0.03</td>
</tr>
<tr>
<td>Brazil 5</td>
<td>41</td>
<td>17.4</td>
<td>1.61</td>
</tr>
<tr>
<td>Brazil 6</td>
<td>127</td>
<td>8.4</td>
<td>2.91</td>
</tr>
<tr>
<td>Brazil 7</td>
<td>16</td>
<td>16.7</td>
<td>0.45</td>
</tr>
<tr>
<td>Brazil 8</td>
<td>43</td>
<td>12.7</td>
<td>2.86</td>
</tr>
<tr>
<td>Brazil 9</td>
<td>81</td>
<td>15.0</td>
<td>1.37</td>
</tr>
<tr>
<td>Chile 1</td>
<td>11</td>
<td>12.6</td>
<td>1.91</td>
</tr>
<tr>
<td>Chile 2</td>
<td>11</td>
<td>15.2</td>
<td>0.86</td>
</tr>
<tr>
<td>Chile 3</td>
<td>2</td>
<td>12.6</td>
<td>0.21</td>
</tr>
<tr>
<td>Chile 4</td>
<td>4</td>
<td>13.4</td>
<td>0.29</td>
</tr>
<tr>
<td>Costa Rica 1</td>
<td>9</td>
<td>11.2</td>
<td>1.64</td>
</tr>
<tr>
<td>Costa Rica 2</td>
<td>9</td>
<td>9.4</td>
<td>1.26</td>
</tr>
<tr>
<td>Cuba 1</td>
<td>5</td>
<td>18.0</td>
<td>4.52</td>
</tr>
<tr>
<td>Cuba 2</td>
<td>12</td>
<td>12.2</td>
<td>3.60</td>
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<td>Cuba 3</td>
<td>10</td>
<td>16.0</td>
<td>3.93</td>
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<tr>
<td>Cuba 4</td>
<td>33</td>
<td>11.3</td>
<td>3.51</td>
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<tr>
<td>Mexico 1</td>
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<td>12.3</td>
<td>0.00</td>
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<tr>
<td>Mexico 2</td>
<td>7</td>
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<td>14.5</td>
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</tr>
<tr>
<td>Mexico 7</td>
<td>80</td>
<td>10.1</td>
<td>4.31</td>
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<tr>
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<td>10.7</td>
<td>0.43</td>
</tr>
<tr>
<td>Other Country 2</td>
<td>1</td>
<td>18.6</td>
<td>0.00</td>
</tr>
<tr>
<td>Other Country 3</td>
<td>39</td>
<td>12.9</td>
<td>0.00</td>
</tr>
<tr>
<td>Uruguay 1</td>
<td>35</td>
<td>16.9</td>
<td>2.49</td>
</tr>
<tr>
<td>Uruguay 2</td>
<td>29</td>
<td>14.9</td>
<td>2.03</td>
</tr>
</tbody>
</table>

(Heterogeneous practice) Lab Volume vs Effective Dose

Figure 2. Distribution of mean laboratory ED by patient volume.

Vitola JV et al J Nucl Cardiol 2016
# Best Practice Adherence by Region

Number (%) of labs adhering to each practice

<table>
<thead>
<tr>
<th>Practice</th>
<th>Africa</th>
<th>Asia</th>
<th>Europe</th>
<th>Latin America</th>
<th>North America</th>
<th>Oceania</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid thallium stress</td>
<td>12(100%)</td>
<td>52(75%)</td>
<td>97(95%)</td>
<td>35(97%)</td>
<td>55(100%)</td>
<td>31(91%)</td>
<td>282(92%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Avoid dual isotope</td>
<td>12(100%)</td>
<td>64(93%)</td>
<td>101(99%)</td>
<td>34(94%)</td>
<td>53(96%)</td>
<td>34(100%)</td>
<td>298(97%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Avoid too much Tc</td>
<td>11(92%)</td>
<td>64(93%)</td>
<td>101(99%)</td>
<td><strong>23(64%)</strong></td>
<td><strong>33(60%)</strong></td>
<td>31(91%)</td>
<td>263(85%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Avoid too much Tl</td>
<td>12(100%)</td>
<td>68(99%)</td>
<td>102(100%)</td>
<td>35(97%)</td>
<td>55(100%)</td>
<td>34(100%)</td>
<td>306(99%)</td>
<td>0.48</td>
</tr>
<tr>
<td>Perform stress-only</td>
<td>8(67%)</td>
<td>16(23%)</td>
<td>47(46%)</td>
<td>7(19%)</td>
<td>9(16%)</td>
<td>6(18%)</td>
<td>93(30%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Use camera based dose reduction strategies</td>
<td>8(67%)</td>
<td>48(70%)</td>
<td>71(70%)</td>
<td>16(44%)</td>
<td>33(60%)</td>
<td>30(88%)</td>
<td>206(67%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Weight based dosing for Technetium</td>
<td><strong>6(50%)</strong></td>
<td><strong>8(12%)</strong></td>
<td><strong>48(47%)</strong></td>
<td><strong>11(31%)</strong></td>
<td><strong>10(18%)</strong></td>
<td><strong>5(15%)</strong></td>
<td><strong>88(29%)</strong></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Avoid “shine through”</td>
<td>7(58%)</td>
<td>26(38%)</td>
<td>66(65%)</td>
<td>14(39%)</td>
<td>8(15%)</td>
<td>15(44%)</td>
<td>136(44%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Relationship between Lab Best Practice Adherence and Predicted Patient ED: Hierarchical Regression Model

<table>
<thead>
<tr>
<th>Best practice/Factor</th>
<th>Reduction in predicted effective dose (mSv)</th>
<th>95% confidence interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid thallium stress</td>
<td>2.54</td>
<td>1.39 – 3.69</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Avoid dual isotope</td>
<td>5.42</td>
<td>3.77 – 7.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Avoid too much technetium</td>
<td>3.12</td>
<td>2.19 – 4.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Avoid too much thallium</td>
<td>1.05</td>
<td>-2.81 – 4.91</td>
<td>0.595</td>
</tr>
<tr>
<td>Perform stress-only imaging</td>
<td>2.28</td>
<td>1.57 – 2.98</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Use camera based dose reduction strategies</td>
<td>1.23</td>
<td>0.58 – 1.88</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight based dosing for technetium</td>
<td>0.84</td>
<td>0.13 – 1.57</td>
<td>0.021</td>
</tr>
<tr>
<td>Avoid “shine through”</td>
<td>-1.03</td>
<td>-1.66 – -0.39</td>
<td>0.002</td>
</tr>
<tr>
<td>Age (years)</td>
<td>-0.004</td>
<td>-0.009 – 0.001</td>
<td>0.142</td>
</tr>
<tr>
<td>Female</td>
<td>0.30</td>
<td>0.18 – 0.43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>-0.04</td>
<td>-0.04 – -0.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intercept (predicted effective dose, mSv)</td>
<td>20.5</td>
<td>16.5 – 24.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

INCAPS Summary

- Marked worldwide variation exists in radiation doses and radiation safety practices pertaining to MPI, e.g.
  - Median lab dose 10.9 mSv, range 2.2-22.4 mSv
  - Mean lab QI score 5, range 2-8

- There is opportunity to improve best practices in most labs
  - Only 3 of 8 best practices used by 90% of labs
  - Only 7% of labs adhered to all 8 best practices
  - Can be implemented without need for special technology or additional costs

- The significant relationship between best practice implementation and lower doses indicates numerous opportunities to reduce radiation exposure from MPI globally

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