It’s all in the Numbers!!!

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Royal Melbourne Hospital
University of Melbourne
Australia

IMIC, Vienna – October 2016
Plan

1. Case History
2. How to quantitate perfusion
3. Other quantitation – it’s not just perfusion
4. Integrating quantitation into YOUR practice
5. Conclusions
Hitchhiker’s Guide to the Galaxy – Deep Thought (Supercomputer)

What is the answer to life, the universe and everything
7.5 million years of work……

Yes, I thought it over quite thoroughly. It's 42.
Conclusion

- Hitch Hiker’s guide to the Galaxy
- The answer is 42 !!!
- But what is the question?
Mr AB

72 year old male
HT, Type 2 diabetic, smoker 15/day
Positive FH, LDL chol 4.1. Prior CVA.
Creat clearance 48 ml/min/1.73m²
Meds – Metformin 1 g bd, Atorvastatin 40 mg

Vague shortness of breath on exertion
Due for aortic aneurysm surgery – stent N/A.
Examination

- Well. 145/85. BMI 32.
- Chest clear
- Otherwise normal

- ECG – SR 80/min. Normal
- CXR - Normal
What would you do?

1. Nothing
2. Ex ECG
3. Stress Echo
4. Stress MRI
5. Cardiac CT
6. Dipyridamole MPI
7. Cath

Let’s see what the guidelines say!!!
**Step 3 - Risk of surgical procedure:**
30-day CV death and MI

<table>
<thead>
<tr>
<th>Low-risk: &lt; 1%</th>
<th>Intermediate-risk: 1-5%</th>
<th>High-risk: &gt; 5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial surgery</td>
<td>Intraproterional: splenectomy, hiatal</td>
<td>Aortic and major vascular surgery</td>
</tr>
<tr>
<td>Breast</td>
<td>hernia repair, cholecystectomy</td>
<td></td>
</tr>
<tr>
<td>Dental</td>
<td>Carotid symptomatic (CEA or CAS)</td>
<td>Open lower limb revascularization</td>
</tr>
<tr>
<td>Endocrine: thyroid</td>
<td>Peripheral arterial angioplasty</td>
<td>or amputation or thromboembolectomy</td>
</tr>
<tr>
<td>Eye</td>
<td>Endovascular aneurysm repair</td>
<td>Duodeno-pancreatic surgery</td>
</tr>
<tr>
<td>Reconstructive</td>
<td>Head and neck surgery</td>
<td>Liver resection, bile duct surgery</td>
</tr>
<tr>
<td>Carotid asymptomatic (CEA or CAS)</td>
<td>Neurological or orthopaedic: major</td>
<td>Oesophagectomy</td>
</tr>
<tr>
<td>Gynecology: minor</td>
<td>(hip and spine surgery)</td>
<td>Repair of perforated bowel</td>
</tr>
<tr>
<td>Orthopaedic: minor (meniscectomy)</td>
<td>Urological or gynaecological: major</td>
<td>Adrenal resection</td>
</tr>
<tr>
<td>Urological: minor (transurethral</td>
<td>Renal transplant</td>
<td>Total cystectomy</td>
</tr>
<tr>
<td>resection of the prostate)</td>
<td>Intra-thoracic: non-major</td>
<td>Pneumonectomy</td>
</tr>
</tbody>
</table>

European Heart Journal (2014) 35, 2383–2431
doi:10.1093/eurheart/jet282
Step 6
Cardiac risk factors in high-risk surgery

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of risk factors ≤2</td>
<td>IIb</td>
<td>B-C</td>
</tr>
<tr>
<td>Rest echocardiography and biomarkers for evaluation of LV function may be considered.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Ischaemic heart disease
2. Heart failure
3. Stroke or TIA
4. Renal dysfunction
5. Diabetes mellitus

Surgery

Number of risk factors ≥3

Step 7

European Heart Journal (2014) 35, 2383–2431
doi: 10.1093/eurheartj/ehu282

www.escardio.org/guidelines
Step 7 – Pre-operative testing

Consider also for patient counselling, surgery, and anaesthesia technique

- **Cardiac stress test**
  - Extensive ischaemia
    - An individualized peri-operative management is recommended considering the potential benefit of the proposed surgical procedure compared with the predicted adverse outcome, and the effect of medical therapy and/or coronary revascularization
  - No or moderate stress-induced ischaemia
    - **Surgery**

0.568 mg/kg IV dipyradramole
Exercise – straight leg raising @ 5 – 9 mins
Inject Tc 99-MIBI @ 7 minutes
75 mg IV aminophylline @ 11 minutes

Normal haemodynamic response
No symptoms
No ECG changes

Pt imaged supine (prone not possible)
Gating + CTAC
LV function - normal

CTAC – No difference
Diagnosis

1. Normal
2. Ischaemia – LAD
3. Ischaemia – Large D1
4. RCA ischaemia
5. RCA infarction
6. Inferior artefact
Calcium Score = 380
Prognostic Value of Calcium Scoring in Addition to SPECT MPI in Symptomatic Patients.
Elsemiek M. et al Circ Imaging 5/16
Management

1. Go ahead with surgery

2. Beta-block first 2/52 – cardiac monitoring

3. Defer surgery and cath
How much ischaemia total?

1. Nil
2. Mild
3. Moderate
4. Severe
Two main coronary Arteries - left and Right - arise from the left and right sinuses of Val-salva. Coronary flow is an essential determine of myocardial function. Left coronary flow is mainly diastolic. Right coronary flow is more evenly spread through systole and diastole. Coronary return - Venous - Coronary Sinus - RA.
Left Ventricular Segmentation

1) Basal anterior  7) Mid anterior  13) Apical anterior
2) Basal anteroseptal  8) Mid anteroseptal  14) Apical septal
3) Basal inferoseptal  9) Mid inferoseptal  15) Apical inferior
4) Basal inferior  10) Mid inferior  16) Apical lateral
5) Basal inferolateral  11) Mid inferolateral  17) Apex
6) Basal anterolateral  12) Mid anterolateral

Short Axis

LAD = Left Anterior Descending
LCX = Left Circumflex artery
RCA = Right Coronary Artery
Each segment is scored on a 5-point scale: 0 = normal perfusion, 1 = mild reduction of tracer uptake (not definitely abnormal), 2 = moderate reduction of uptake (definitely abnormal), 3 = severe reduction of uptake, and 4 = absence of uptake.\textsuperscript{19}

<table>
<thead>
<tr>
<th>Summed Stress Score</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 4</td>
<td>Normal</td>
</tr>
<tr>
<td>4-8</td>
<td>Mildly abnormal</td>
</tr>
<tr>
<td>9-13</td>
<td>Moderately abnormal</td>
</tr>
<tr>
<td>&gt; 13</td>
<td>Severely abnormal</td>
</tr>
</tbody>
</table>

- The summed stress score (SSS) is obtained by adding the individual scores derived from the 17 segments during stress and represents the amount of both ischemia and infarct in the left ventricular myocardium.
- The summed rest score (SRS) is the sum of the individual scores during rest and represents the amount of infarcted left ventricular myocardium.
- Summed difference score (SDS) = SSS – SRS and represents the amount of reversibility between stress and rest reflecting the amount of ischemia in the left ventricular myocardium.\textsuperscript{19}
Predictive value of exercise myocardial perfusion imaging in the Medicare population: the impact of the ability to exercise.

Kwon et al Cardiovasc diagnosis and therapy. Feb 2014

### Table 3 Revascularization rates stratified by summed stress score

<table>
<thead>
<tr>
<th>SSS</th>
<th>Total # abnormal</th>
<th>Rate of 90 day revascularization [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSS =0-2</td>
<td>39</td>
<td>1 [2.6]</td>
</tr>
<tr>
<td>SSS =3-4</td>
<td>88</td>
<td>11 [12]</td>
</tr>
<tr>
<td>SSS &gt;4</td>
<td>446</td>
<td>109 [24]*</td>
</tr>
</tbody>
</table>

*, Chi-square with two degrees of freedom =14.94, P=0.0006.
#, number of patients.

Maximal MET was a better predictor of survival!!
What is the SSS?

<table>
<thead>
<tr>
<th>Segment</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>2</td>
</tr>
</tbody>
</table>

**SSS 32**
Lots of options for quantitation !!

• Perfusion – SSS, SRS, SDS
• Function – LVEF, regional, wall thickness, diastole

• Semi-quantitative i.e you do it yourself!!
• Cedar – Sinai
• Emory tool box
• 4D – SPECT – good for getting your own lab normal data base, incl prone

In Australia, some of our patients are different to yours ……
Australia’s Response for Preventing the Metabolic Syndrome: Walking the Dog
Extent and severity = total perfusion deficit – Beware of “small area of severe ischaemia v. Large area of mild ischaemia”
17 – segments now preferred !!
You must always QC Quatitation!!!!

How do you use it clinically?

NEVER ALONE !!!

THIRD UMPIRE!!
Sources of variability of gated myocardial perfusion SPECT quantitative parameters E. Gordon DePuey  JNC 8/16
Sources of variability of gated myocardial perfusion SPECT quantitative parameters

E. Gordon DePuey  JNC 8/16

Radiopharmaceutical Radionuclide (Tc-99m, TI-201)
Injected activity (low-dose, high-dose)
Hardware Camera spatial resolution (NaI, CsI, CZT)
Energy resolution (NaI, CsI, CZT)
Collimator In-plane linear resolution
Depth-dependent resolution (cardio-focused, multipinhole collimators)
Attenuation correction (high-flux CT, low-flux CT, Gd- 153)
Software Filtering (filtered backprojection, iterative reconstruction, none)
Myocardial edge detection
Resolution recovery
Noise reduction/modulation
Quantitative analysis
Comparison with software-specific normal limits
Patient-related factors Gender Body habitus Soft tissue attenuation
Scatter Position for imaging (supine, upright, semi-upright)
Heart rate.
• How does this data help our patient?

• It’s “All in the Numbers”!!!!
  — Not just a simple bull’s eye!!
15-Year outcome after normal exercise 99mTc-sestamibi myocardial perfusion imaging: What is the duration of low risk after a normal scan?

<table>
<thead>
<tr>
<th>Event</th>
<th>Annualised event rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>1.1%</td>
</tr>
<tr>
<td>Cardiac mortality</td>
<td>0.3 %</td>
</tr>
<tr>
<td>Cardiac death/MI</td>
<td>0.7 %</td>
</tr>
<tr>
<td>Major cardiac event rate</td>
<td>1.8 %</td>
</tr>
</tbody>
</table>

Schinkel et al JNC 6/12
15-Year outcome after normal exercise 99mTc-sestamibi myocardial perfusion imaging: What is the duration of low risk after a normal scan? 

Schinkel et al JNC 6/12

14 year F/U dob MIBI – good predictor JNC 12/15
Dobutamine stress myocardial perfusion imaging: 8-year outcomes in patients with diabetes mellitus

Hendrik J. Boiten et al.... EHJ CI 7/16

n = 194 diabetics, unable to exercise had dobutamine MPI

8.1 +/- 5.9 year F/U
134 died, 68 cardiac death
24 non-fatal MI
61 late revasc @ 60 days
Dobutamine stress myocardial perfusion imaging: 8-year outcomes in patients with diabetes mellitus

Hendrik J. Boiten et al.... EHJ CI 7/16

A - All cause Mortality – prognostic value lost after 4 years

B - Cardiac Mortality

C - Hard Cardiac Events
But what is important???

• In 1980, the question was “Ischaemia – Yes or no?”

• In 2016, the question is “How does it change management – How much ischaemia?”
Comparison of short time survival with Revascularisation v. Medical Therapy

Hachamovitch et al. Circ 6/03

n = 10,627 pts
No prior CAD. Ex or adenosine sestamibi SPECT
Treatment within 60 days
671 pts revasc v. 9956 pts medical Rx
146 patients died
90.6 % patients followed for 1.9 ± 0.6 years
Comparison of short time survival with Revascularisation v. Medical Therapy

Hachamovitch et al  Circ 6/03

C.D rate (%)

% Ischaemic myocardium

Medical Rx
Revascularisation

* p < 0.0001
Comparison of short time survival with Revascularisation v. Medical Therapy

Hachamovitch et al. Circ 6/03

Conclusions

Survival benefit for revascularisation if –
> 12.5 % myocardium ischaemic
high risk patients (elderly, women, diabetics)

SDS > 8 !!
ISCHAEMIA trial

- n = 8000
- Commenced July 2012 .... Results ? 2017
- Mod – severe ischaemia

- OMT v revascularisation
<table>
<thead>
<tr>
<th>Outcome (% predicted METs achieved)</th>
<th>Adjusted hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td></td>
</tr>
<tr>
<td>&lt;85</td>
<td>2.36 (1.55–3.60)</td>
</tr>
<tr>
<td>85–100</td>
<td>0.79 (0.46–1.36)</td>
</tr>
<tr>
<td>&gt;100</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td></td>
</tr>
<tr>
<td>&lt;85</td>
<td>2.39 (1.78–3.21)</td>
</tr>
<tr>
<td>85–100</td>
<td>1.31 (0.94–1.81)</td>
</tr>
<tr>
<td>&gt;100</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>CABG, PCI</td>
<td></td>
</tr>
<tr>
<td>&lt;85</td>
<td>1.75 (1.46–2.08)</td>
</tr>
<tr>
<td>85–100</td>
<td>1.08 (0.90–1.31)</td>
</tr>
<tr>
<td>&gt;100</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td></td>
</tr>
<tr>
<td>&lt;85</td>
<td>2.90 (1.88–4.47)</td>
</tr>
<tr>
<td>85–100</td>
<td>1.08 (0.90–1.31)</td>
</tr>
<tr>
<td>&gt;100</td>
<td>1 (reference)</td>
</tr>
</tbody>
</table>

Incremental prognostic value & exercise SPECT

% CER

- Normal
- Mild
- Severe

Duke Treadmill Score

Low risk
Intermediate
High risk

2200 pts
Rest thallium-201/
Stress Tc99m MIBI

Cath rate -
Very similar data

Hachamovitch et al ... Circ 3/9
Cardiac Prognosis - Gating & Risk

Sharir et al.….JNM 6/01

2686 pts over approx 3 years
Rest thallium-201/stress Tc-99m MIBI
Quantitative perfusion - SSS, SRS and SDS
Automated post-stress LVEF
? Cardiac death and MI rate
Cardiac Prognosis - Gating & Risk

Sharir et al….JNM 6/01

Best predictor of
CD = Post stress LVEF
non fatal MI = Amount ischaemia

Cardiac death
% per year

Also SCD-Heft / MADIT 2

What extra info do we need???
First, ....... The Holy Grail

Who gets an AICD???

Maybe NOT EF < 35 % in non-ischaemic CM (ESC 9/16)
ADMIRE – HF

• n = 961 over 2 years
• LVEF < 35 %
• I-123 MIBG. Cardiac uptake quantitated.
• 237 pts had events
• Change in NYHA class, cardiac death or serious arrhythmia.
< 1.6
Review of Nuclear Cardiology Practices and Radiation Exposure in the Oceania Region: Results from the IAEA Nuclear Cardiology Protocols Study (INCAPS)


Heart, Lung and Circulation.
September 2016
Very low-activity stress/high-activity rest, single-day myocardial perfusion SPECT with a conventional sodium iodide camera and wide beam reconstruction processing

E. Gordon DePuey MD, Pashmina Ata MD, Rick Wray MD, Marvin Friedman PhD

JNC 10/12

Combining new software and stress only imaging, can get dose approx 1.4 mSv
Method

Eight “best practices” pre-determined by IAEA expert panel to reduce radiation dose

Each lab given quality index (QI) score (0-8) according to number of “best practices”

“Best practices”

1. Avoid thallium stress if < 70
2. Avoid dual isotope
3. Avoid too much technetium
4. Avoid too much thallium
5. Perform stress-only imaging
6. Use of camera-based dose-reduction strategies
7. Weight-based dosing for technetium
8. Avoid inappropriate dosing that can cause “shine-through” artifact
## Results

<table>
<thead>
<tr>
<th></th>
<th>Oceania</th>
<th>Rest of the World</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labs</td>
<td>34</td>
<td>274</td>
<td></td>
</tr>
<tr>
<td>MPI Studies</td>
<td>439</td>
<td>7472</td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td>45.1</td>
<td>40.9</td>
<td>0.08</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>65.4 ± 12.6</td>
<td>64.1 ± 11.9</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>83.0 ± 20.1</td>
<td>80.2 ± 18.7</td>
<td>0.16</td>
</tr>
<tr>
<td>Mean effective dose (mSv)</td>
<td>9.3 ± 3.7</td>
<td>10.0 ± 4.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Proportion of patients receiving dose ≤ 9 mSv (%)</td>
<td>36.7</td>
<td>30.7</td>
<td>0.23</td>
</tr>
</tbody>
</table>
Worldwide Variation in Nuclear Cardiology Practice – Quality Index
## Results

### Within Oceania

<table>
<thead>
<tr>
<th></th>
<th>Metropolitan</th>
<th>Non-Metropolitan</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labs</td>
<td>22</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>MPI Studies</td>
<td>335</td>
<td>104</td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td>44.2</td>
<td>48.1</td>
<td>0.49</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>$65.6 \pm 12.6$</td>
<td>$64.9 \pm 12.6$</td>
<td>0.63</td>
</tr>
<tr>
<td>Mean effective dose (mSv)</td>
<td>$8.9 \pm 3.8$</td>
<td>$10.6 \pm 2.8$</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Proportion of patients receiving dose $\leq 9$ mSv (%)</td>
<td>40.9</td>
<td>23.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean QI score</td>
<td>$5.5 \pm 0.7$</td>
<td>$5.4 \pm 0.8$</td>
<td>0.75</td>
</tr>
<tr>
<td>Stress only studies (%)</td>
<td>15.2</td>
<td>3.8</td>
<td>0.002</td>
</tr>
</tbody>
</table>
INCAPS Oceania Conclusions

1. Mean effective dose from MPI lower in Oceania than rest of the world
2. However, only 36.7% of studies performed with dose \( \leq 9 \text{ mSv} \) in Oceania
3. Oceania labs comparable if not better than rest of world in adherence to “best practices”
4. Radiation dose higher in non-metropolitan compared to metropolitan laboratories in Oceania
Quantitating old things - Coming back

GBPS – low dose, SPECT, CZT technology

VQ scans – renal impairment, chronic pulmonary hypertension investigation (ESC guidelines 2015)
SPECT - 0.5 v 2 segments mismatch

Bone/pyrophosphate scans - amyloid
Representative Image of a Whole-Body Scan by $^{99m}$Tc-DPD Scintigraphy
Detection of technetium-$^{99m}$-3,3-diphosphono-1,2-propanodicarboxylic acid ($^{99m}$Tc-DPD) heart retention in a patient with a Val20Ile variant of the transthyretin gene.
Early Phase $^{99}$Tc-HMDP Scintigraphy for the Diagnosis and Typing of Cardiac Amyloidosis

(A) Agreement between (C/M) and Perugini’s visual score. (B) Proposed diagnostic algorithm for patients with suspected cardiac amyloidosis (CA). AL = light-chain amyloidosis; C = cardiac; H = heart; H/M = heart-to-mediastinum; HMDP = hydroxyl-methylene-diphosphonate; LVH = left ventricular hypertrophy; m-TTR-CA = hereditary transthyretin-related cardiac amyloidosis; SPECT = single-photon emission computed tomography; TTR = transthyretin-related; wt-TTR-CA = wild-type transthyretin-related cardiac amyloidosis.
New things 2016

Cardiac PET – potentially for personalised medicine (Dilsizian... JNC 6/16)

- FDG – viability, sarcoid
- New agents - amyloid
- Rubidium-82
- CFR
- F-18 Flurpiridaz
- Vulnerable plaque – FDG, Na F (Joshi et al)
Representative $^{11}$C-PiB PET/CT Images of the Study Participants

(A) Diffuse, homogeneous uptake pattern in patient 9. The uptake of $^{11}$C-PiB was noted at both the LV and RV. Subendocardial ring enhancement pattern was noted at the late gadolinium enhancement (LGE)-cardiac magnetic resonance (CMR) image. (B) Heterogeneous uptake pattern in patient 5. Although there was uptake noted at other regions, the uptake of $^{11}$C-PiB was more strongly positive at the inferoseptum and, to a lesser degree, at the lateral segment. Heterogeneous transmural enhancement pattern was present at the LGE-CMR image. (C) A representative $^{11}$C-PiB positron emission tomography (PET)/computed tomography (CT) image of a patient who had undergone chemotherapy before $^{11}$C-PiB PET/CT (Patient #12). The $^{11}$C-PiB uptake was marginally elevated, and LGE-CMR demonstrated a subendocardial ring enhancement pattern. (D) A representative negative $^{11}$C-PiB PET/CT scan image of a patient who did not have cardiac amyloidosis (Patient #18). The LGE-CMR image was also normal.
Coronary flow reserve (CFR)

Global Coronary Flow Reserve Is Associated With Adverse Cardiovascular Events Independently of Luminal Angiographic Severity and Modifies the Effect of Early Revascularization

Viviany R. Taqueti, MD, MPH; Rory Hachamovitch, MD, MS; Venkatesh L. Murthy, MD, PhD; Masanao Naya, MD, PhD; Courtney R. Foster, MS; Jon Hainer, BS; Sharmila Dorbala, MD, MPH; Ron Blankstein, MD; Marcelo F. Di Carli, MD

January 2015, Circulation

Groups from Brigham and Women’s Hospital, Harvard, Boston MA, Cleveland Clinic, OH and University of Michigan

Magic number > 2.5 – Global v regional
So what about our patient

- What would you do?
- Calcium score high
- Ischaemia = large
- LVEF = good
- Defer Surgery and cath v beta blocker
- Let’s Vote
So... It’s all in the Numbers

- 12.5 % ischaemia
- SSS > 8
- 85 % for predicted exercise capacity
- 35 % LVEF for AICD
- < 1.6 for H:M ratio MIBG
- 1.2 for H:M ratio for amyloid
- 2.5 for CFR
- 4 year prognosis at worst for a normal scan
- Calcium score esp > 100 = bad (> 0 to change Mx)
- Radiation safety - Keep it < 9 mSv
12.5 \times 8 \times 0.85 \times 0.35 \\
x 1.6 \times 1.2 - 2.5 - 4 \times \\
100\% - 9 = ??????????
CONCLUSION

The answer is

42 !!!!!!!

But sometimes the answer is not as simple as 1, 2, 3 .................
My Home !!!

THE UNIVERSITY OF MELBOURNE