PET/MR: A COMMERCIAL SUCCESS STORY?

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Forbes
TOPICS

1. Current Situation,
2. Causes & Effects,
3. Possible Solutions(?)

DISCLAIMER: This presentation represents the speaker's own beliefs, which may be different from Philips' and/or AIPES' formal positions.
MOLECULAR IMAGING

Very promising but at the same time Very Difficult to Grow — WHY?

• Radioactivity

• Cumbersome Logistics

• Heavily relies on Radiopharmaceuticals
  • Similar to Pharmaceutical Industry Innovation cycle – heavy investment
  • Much smaller market – low ROI

• Small Companies → Small Expectations / Big Companies → Great Expectations
  • Consolidation of MI devices producers into big conglomerates ~15yrs ago
Very promising but at the same time Very Difficult to Grow – WHY?

- Radioactivity – Even more So! (higher energies)

- Cumbersome Logistics (= Cyclotrons! Or expensive Generators)

- Heavily relies on Radiopharmaceuticals
  - Similar to Pharmaceutical Industry Innovation cycle – heavy investment
  - Much smaller market – low ROI

- Small Companies → Small Expectations / Big Companies → Great Expectations
  - Consolidation of MI devices producers into big conglomerates ~15yrs ago
  - Consolidation of Profit Centres inside big conglomerates → focus of investment goes where there is revenue
PET/MR IMAGING

Very promising but at the same time Very Difficult to TAKE OFF

Identity issues
- Is it an improved PET/CT? Is it a molecular MRI?
- Who owns it? Nuclear Medicine? Radiology?

Cost/Benefit issues
- High upfront investment (scanner/room/infrastructure)
- High running costs
- Difficult Return on Investment

Technology Issues
- Is it ready?
- Is this how it should look like?
Diagnostic facilities by hospital size (USA)

(Medical Options, 2012)

(Burns, 2010)
THE PEDIGREE OF PET

1953
Brownell and Sweet. First PET images with 74As. (Nucleonics 1953, 11:40-45)

1966
H.O.Anger's Description of TOF

1973
The MGH Positron Camera PC-I

1982
Early TOF PET scanner, SuperPETT I

1999
First PET/CT Prototype

2006
First clinical whole-body TOF-PET/CT GEMINI TF

Early 90s
First Commercial PET Scanners

2010-2014 PET/MR

2013
SiPM-TOF-PET/CT

2014
BGO PET/CT

A range of state-of-the-art PET/CT systems
SOME PREVIOUS FAILED DIFFERENTIATION ATTEMPTS IN MOLECULAR IMAGING

- ECAT HRRT
  - Niche Market Segment
- IMMATURITY TECHNOLOGY
  - Introduction of FDG
- SUPER PETT I
  - (1st Gen TOF-PET)
- PETRRA
  - Very Late In The Market
- ISOCAM
  - Design Issues
  - Accidents
- PRECEDENCE
  - High Production Cost
  - Design Issues
- BrainPET MR insert
  - Small Market Segment
  - Early For Product Bifurcation
CURRENT PET/MR USER PROFILE

Who is it you work with?

- Radiographer/Tech...
- Nurse
- Doctor
- Researcher
- Other

Does your site have other MRI scanners?

- Other [8]
- 4 [9]
- 0 [1]
- 1 [1]
- 2 [2]
- 3 [4]

Does your site have other PET scanners?

- Europe [18]
- America [2]
- Asia [5]
- 2 [11]
- 3 [4]
- 4 [0]
- Other [2]
- 0 [0]

* 2013

Data courtesy of Dr John J Totman
A-Star/Singapore
PET/MR CURRENT MARKET SIZE

Anticipated but not necessarily materialised within 2015

Global PET/MR Market

Install Base ~69
Orders ~15
Expected but not confirmed ~50
TOTAL ~134

Market Growth

- 2011: 34 Systems (2 Manufacturers)
- 2012: 47 Systems (2 Manufacturers)
- 2013: 68 Systems (2 Manufacturers)
- 2014: 83 Systems (3 Manufacturers)
- 2015: 84 Systems (3 Manufacturers)
- 2015+: 50 Systems (4 Manufacturers + 2 niche?)

* April 2015
GREAT SUCCESS
Uncertainty about:
- achievable market volumes
- Length of adoption phase
  - Transition to Early Majority
  - Customer Identity

Reactions:
- Technological stalling
- Divestment of resources
- Aggressive penetration attempts

Slow development
TECHNOLOGY DISSEMINATION

The three triangles model: More for less for more for less*

Type of Innovation
- Technology led
- Product-based
- First in the world
- e.g., iPad

Level of Visibility
- High
- Low

Societal Impact
- MR/LinAc
- 7T MRI
- PET/MR
- PET/CT
- MRI
- X-Ray

*More benefits with less visibility for more people at less cost

Adapted from “Accenture Democratizing Innovation Report 2011”
MARKET FORCES & PET/MR PRICE

- Threat of New Entrants
  - NOT IMMEDIATE THREAT BUT...
    - United Imaging
    - Samsung?
    - Joint Ventures?

- SIEMENS
  - Rivalry Among Existing Competitors
  - Bargaining Power of Suppliers
  - Bargaining Power of Buyers
  - Threat of Substitute Products or Services
  - Investment risk premium

- Other capital equipment purchases
- Reimbursement vs other modalities

- PET/CT+MRI?

- 7m EUR
- 5m EUR
- 4m EUR
- 3.5m EUR
- 3.5m EUR

**ENVIRONMENTAL SETTINGS FOR ADOPTION**

<table>
<thead>
<tr>
<th>ENVIRONMENTAL DIFFICULTIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conservative &amp; Highly-Regulated Market</td>
</tr>
<tr>
<td>Inherent Characteristics of Disruptive Innovation</td>
</tr>
<tr>
<td>Complicated Stakeholder Structure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CONSERVATIVE &amp; HIGHLY REGULATED MARKET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulated wrt its use (indications/users)</td>
</tr>
<tr>
<td>Regulated wrt its reimbursement</td>
</tr>
<tr>
<td>Occasionally Regulated also wrt population that serves</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MULTIDIMENSIONAL DISRUPTIVE TECHNOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technological Breakthrough</td>
</tr>
<tr>
<td>(detectors/MRAC/recon/motion/…)</td>
</tr>
<tr>
<td>Organisational Breakthrough</td>
</tr>
</tbody>
</table>

Kalemis (2011)
DISCONTINUOUS INNOVATION IN HEALTHCARE ORGANISATIONS

Results are not obvious in the short-term and any Return On Investment is lying further in the future making the investment of resources riskier.

Very difficult to manage/maximise value as the majority of Operations are based on models tailored for incremental innovation conditions (Phillips et al., 2006).

- e.g. An improved MRI scanner may clearly demonstrate better DWI – is it so clear with PET/MR in the eyes of a radiologist?
- e.g. Reimbursement almost non-existent

Although care-chain collaborations enhance incremental innovation, defined Structures may inhibit discontinuous innovation (Utterback, 1996).

- e.g. With a new PET/CT or MRI you still need the same clinical team, but with PET/MR radical changes are necessary.
### Stakeholder Structure

<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Power</th>
<th>Legitimacy</th>
<th>Urgency</th>
<th>Risk Bearing</th>
<th>Stakeholder Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiologists</td>
<td>N</td>
<td>1/O</td>
<td>T/C</td>
<td>Y</td>
<td>Definitive/Direct</td>
</tr>
<tr>
<td>NM Physicians</td>
<td>N</td>
<td>1/O</td>
<td>T/C</td>
<td>V</td>
<td>Definitive/Direct</td>
</tr>
<tr>
<td>Faculty Physicians (Internal)</td>
<td>N</td>
<td>1/O</td>
<td>C</td>
<td>V</td>
<td>Dangerous/Direct</td>
</tr>
<tr>
<td>Medical Physicians</td>
<td>N</td>
<td>1/O</td>
<td>T/C</td>
<td>V</td>
<td>Dependent/Direct</td>
</tr>
<tr>
<td>Referring Physicians (External)</td>
<td>U</td>
<td>S</td>
<td>-</td>
<td>Y</td>
<td>Dormant/Direct</td>
</tr>
<tr>
<td>Imaging Dept. Managers</td>
<td>U</td>
<td>O</td>
<td>C</td>
<td>V</td>
<td>Dangerous/Direct</td>
</tr>
<tr>
<td>Clinical Academic Groups</td>
<td>U</td>
<td>O/S</td>
<td>-</td>
<td>V</td>
<td>Dangerous/Direct</td>
</tr>
<tr>
<td>Hospital Administration</td>
<td>U</td>
<td>O</td>
<td>C</td>
<td>V</td>
<td>Definitive/Direct</td>
</tr>
<tr>
<td>Investors (Private)</td>
<td>U</td>
<td>I</td>
<td>C</td>
<td>V</td>
<td>Dominant/Direct</td>
</tr>
<tr>
<td>Research Funding Bodies</td>
<td>U</td>
<td>S</td>
<td>-</td>
<td>V</td>
<td>Dormant/Direct</td>
</tr>
<tr>
<td>Professional Associations</td>
<td>N</td>
<td>S</td>
<td>C</td>
<td>I</td>
<td>Demanding/Indirect</td>
</tr>
<tr>
<td>Gov/nt Advisory Bodies</td>
<td>N</td>
<td>S</td>
<td>T/C</td>
<td>I</td>
<td>Definitive/Indirect</td>
</tr>
<tr>
<td>Manufacturers</td>
<td>U</td>
<td>S</td>
<td>T/C</td>
<td>Y</td>
<td>Discretionary/Direct</td>
</tr>
<tr>
<td>Governments</td>
<td>N/U</td>
<td>S</td>
<td>-</td>
<td>I</td>
<td>Dormant/Indirect</td>
</tr>
<tr>
<td>“Innovators”</td>
<td>N</td>
<td>1/O/S</td>
<td>T/C</td>
<td>V</td>
<td>Demanding/Direct</td>
</tr>
</tbody>
</table>

Kalemis (2011)
Comparison is the thief of Joy

~Theodore Roosevelt
HOSPITALS PERSPECTIVE: PET/MR VS. MRI

<table>
<thead>
<tr>
<th>#</th>
<th>Benefits for PET/CT vs stand-alone PET</th>
<th>Nature</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Revolution in patient throughput → Profitability of Department</td>
<td>Economical</td>
</tr>
<tr>
<td>2</td>
<td>By linking PET to CT it popularised the former, across referring physicians.</td>
<td>Political</td>
</tr>
<tr>
<td>3</td>
<td>Easier understanding of scans and interpretation by non-expert physicians.</td>
<td>Political</td>
</tr>
<tr>
<td>4</td>
<td>Better reporting due to the use of anatomical CT information to explain functional anomalies on the PET.</td>
<td>Clinical</td>
</tr>
<tr>
<td>5</td>
<td>Low Dose CT results in suboptimal quality for CT diagnosis. → Not chargeable → No loss of revenue for Radiology</td>
<td>Political</td>
</tr>
</tbody>
</table>

One more Issue

MRI Reimbursement inadequate for PET component

Economical

...one more

MRI is inherently an organ imager while PET/CT a whole-body imager (at least up until now!)

Clinical

...and a final one

A one stop-shop approach for PET+MRI feasible only when prescribed as such. Today in most cases an inconclusive MRI (or CT) leads to a PET/CT scan.

Economical

Clinical

<table>
<thead>
<tr>
<th>MRI</th>
<th>Q4 2014 vs 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2013</td>
</tr>
<tr>
<td>Average number of scan-based systems</td>
<td>2145</td>
</tr>
<tr>
<td>Scans per system per day</td>
<td>8.46</td>
</tr>
<tr>
<td>Total number of scan-based MRI scans</td>
<td>120,450</td>
</tr>
<tr>
<td>Price per scan</td>
<td>349</td>
</tr>
<tr>
<td>Scan-based MRI revenue (in millions)</td>
<td>42.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PET/CT</th>
<th>Q4 2014 vs 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2013</td>
</tr>
<tr>
<td>Average number of systems</td>
<td>11131</td>
</tr>
<tr>
<td>Scans per system per day</td>
<td>5.45</td>
</tr>
<tr>
<td>Total number of PET/CT scans</td>
<td>35,245</td>
</tr>
<tr>
<td>Price per scan</td>
<td>945</td>
</tr>
<tr>
<td>Total PET and PET/CT revenue (in mil)</td>
<td>34.5</td>
</tr>
</tbody>
</table>

Published Quarterly results of ALLIANCE IMAGING (USA)
## Hospitals Perspective: PET/MR vs. PET/CT

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<th>Met in PET/MR vs PET/CT?</th>
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<td>Revolution in patient throughput → Profitability of Department</td>
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<td>NO</td>
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<td>2</td>
<td>By linking PET to CT it popularised the former, across referring physicians.</td>
<td>Political</td>
<td>POTENTIALLY YES</td>
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<td>3</td>
<td>Easier understanding of scans and interpretation by non-expert physicians</td>
<td>Political</td>
<td>NO</td>
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<td>4</td>
<td>Better reporting due to the use of anatomical CT information to explain functional anomalies on the PET.</td>
<td>Clinical</td>
<td>BETTER IN SOME CASES (HOW MUCH BETTER?)</td>
</tr>
<tr>
<td>5</td>
<td>Low Dose CT results in suboptimal quality for CT diagnosis. → Not chargeable → No loss of revenue for Radiology</td>
<td>Political</td>
<td>NO</td>
</tr>
</tbody>
</table>

### One more Issue
- PET/CT Reimbursement inadequate for PET/MR throughput
  - Nature: Economical

### ...and a final one
- A one stop-shop approach for PET+MRI feasible only when prescribed as such. Today in most cases an inconclusive MRI (or CT) leads to a PET/CT scan.
  - Nature: Economical / Clinical
VALUE CREATION & ROI: PET/MR VS. PET/CT

PET/MR Costs
- Equipment Costs (3-4.5 million euros)
- Space Costs (1.5 million euros)
- Staff Cost (2 staffs)
- Operational Costs/Year (1.1-1.25 million euros)
- Consumables (FDG) (350-750 euros)

PET/MR Overall Cost Saving
- Cost Benefits for Outpatients
- Profitability of the hospital is related to "Quantity" of scans
- No direct time-saving benefit
- No direct FDG saving benefit
- No direct cost saving

If an outpatient hospital considers investing either PET/CT or PET/MR, PET/CT seems to be a more lucrative alternative, granted that there is sufficient throughput for PET/CT.

POTENTIAL
What is the Δ vs PET/CT?

Courtesy of Philips Healthcare
CLINICAL EFFICACY — DIFFERENCES IN MODALITIES

- PET(MR) Quantification is not solved yet

- CT already provides detailed anatomy & morphology for cancer staging, (...) ➔
  - the step from FDG PET/CT to FDG PET/MR is much more incremental than from FDG PET to FDG PET/CT.

- It may be arguable whether MRI can replace CT or whether the additional information from MRI imaging justifies the substantially higher costs of FDG PET/MRI.

- CT is much more standardised than MRI

(Weber, JNM 2014)
CLINICAL EFFICACY — REGULATORY ENVIRONMENT

EXAMPLE:

- Increased diagnostic accuracy by 30%
- Treatment changes in patients 50%
- Improved outcomes in patients 30%

CONSEQUENCE:

Randomised clinical trials of several hundreds of patients will be needed.

Each for a specific indication
(e.g. Preoperative staging of II breast cancer followed by surgery)

(Weber, JNM 2014)
CLINICAL EFFICACY — IN SEARCH OF PROOFS

• Most PET/MR studies are compared to FDG PET/CT, both imaging acquired sequentially with one injection. Such design may not necessarily identify the most promising clinical applications.

• Most PET/MR studies are done for applications where CT is considered to provide at least as good diagnostic information as MRI. (Room for improvement?)

• Future studies should focus to other studies than WB FDG PET/MR vs PET/CT.

• New highly specific tracers need much better soft tissue contrast - hence PET/MR?

(Weber, JNM 2014)
IS CURRENT RESEARCH AIMING AT THE RIGHT DIRECTION?

No, but we are slowly getting there.
SUMMARY OF THE ADOPTION BARRIERS

<table>
<thead>
<tr>
<th>SACRIFICES REQUIRED BY ADOPTERS</th>
<th>LACK OF INCENTIVES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COST</strong></td>
<td></td>
</tr>
<tr>
<td>Capital Investment</td>
<td>Clinical indications where PET/MR is better clinically &amp; economically are missing today</td>
</tr>
<tr>
<td>Running costs</td>
<td>Lack of Reimbursement for joint PET/MR scans</td>
</tr>
<tr>
<td>More expensive scans vs. PET/CT or MRI</td>
<td>“Unproven” hybrid technology</td>
</tr>
<tr>
<td>Competition vs. other modalities for research grants</td>
<td></td>
</tr>
<tr>
<td><strong>INFRASTRUCTURE</strong></td>
<td></td>
</tr>
<tr>
<td>Highly trained personnel.</td>
<td></td>
</tr>
<tr>
<td>Logistics: Space, Location in relation to NM and Radiology, etc</td>
<td></td>
</tr>
<tr>
<td>Scanner Environment: Strong magnetic fields &amp; Radiation</td>
<td></td>
</tr>
<tr>
<td><strong>CULTURE</strong></td>
<td></td>
</tr>
<tr>
<td>NM vs. Radiology struggle</td>
<td></td>
</tr>
<tr>
<td>Adoption of new tool by faculty physicians to refer patients</td>
<td></td>
</tr>
</tbody>
</table>

Kalemis (2011)
ADOPTION — CURRENT STATUS

"Hype Cycle" model, Gartner 1995
"Technology Adoption Lifecycle", Rogers & Moore
PARADIGM SHIFT IN MEDICAL IMAGING

- Diseased cells release biological markers
- First symptoms/manifestation
- Probability of Mortality
- Treatment costs
- Acceptable Cost of Diagnostics
- Expected Accuracy of Diagnostics
- Therapy planning aids
- Disease proliferation
- PET/MR Niche?
HOW TO ‘JUMP’ THIS GAP?

PET
* Approval of New tracers for clinical use.

MRI
* Transition of “Research” applications into clinical practice.
* “Standardisation” of MR protocols per disease.

PET/MR
* Improved Quantification
* Optimisation of MR equipment (coils, couch,…) to reduce photon attenuation & scatter and facilitate whole-body scans.
* Reduce acquisition times
* Meet modern MRI standards (e.g. wide bore)

Medical Informatics
* Analysis, Fusion and Display of complex data structures.

Medical Accreditations for NM and Radiology Physicians/Radiographers

Clinical Evaluation
* Focus clinical studies not on low-hanging fruits but on end-goals to support +ve HTAs and result into reimbursable procedures
“A likely impossibility is always preferable to an unconvincing possibility.”
Aristotle

“Behold the turtle. He makes progress only when he sticks his neck out.”
James Bryant Conant

THANK YOU