The integration of functional imaging in the management of head and neck cancer

Sandro V Porceddu
Director, Radiation Oncology Research
Princess Alexandra Hospital, Brisbane, Australia
Professor, Faculty of Medicine, University of Queensland
Head and Neck PET Imaging Research Program

- Clinical research program assessing the utility of functional (PET/CT) imaging in the evaluation of the neck following radiotherapy in head and neck cancer

- Incorporation of the findings into the routine management of head and neck cancer
5-year relative survival (per cent)

5 year survival in:
- 1986 44%
- 2016 70%

New cases/deaths per 100,000
Progress in Cancer Care

- Screening & Prevention
- Databases
- Multidisciplinary Care
- Clinical Trials
- Personalised Therapy
- Targeted Therapy
- Immunotherapy

Progress in Cancer Care
Multidisciplinary Care

Patient-centred Care

Surgeon
Medical Oncologist
Radiation Oncologist
Pathologist
Radiologist
Nurse/Research Nurse
Allied Health
Palliative Care Physician
Psycho-oncologist
Data-manager
Scientist/Researcher
Multidisciplinary Care

Surgeon
Medical Oncologist
Radiation Oncologist
Pathologist
Radiologist
Nurse/Research Nurse
Allied Health
Palliative Care Physician
Psychoncologist
Scientist/Researcher
Data-manager
Mucosal Head and Neck Cancer
Head and Neck Cancer

- 4-6% of all cancers
- 5% of cancer-related deaths
- Commonly Squamous Cell Carcinoma
- Smoking related
Falling rates of smoking

Sturgis and Ang, JNCCN, 2011
Rising incidence of Oropharyngeal SCC

Fig. 3. The incidence of laryngeal and oropharyngeal carcinomas in Denmark 1977–2007.
Rising incidence or HPV associated Oropharyngeal Ca

- HPV16+

SEER Registry

Ernster JA et al, Laryngoscope 2007
Treatment

Options
• Surgery/post-operative radiotherapy
• Chemo-radiotherapy
• No randomised comparisons

Outcomes
• 40-60% 3yr overall survival
• (85% 3yr OS HPV+ disease)
Curative chemo-radiotherapy
Node positive head & neck cancer

- 7 weeks of XRT & concurrent cisplatin
Icarus effect
Residual nodal dilemma following radio(chemo)therapy

- 40-50% of patients with node positive Head & Neck SCC will have a residual nodal abnormality after radiotherapy
Management of the neck following Radiation Therapy and a complete response at the primary site

- Following a complete response in the neck - isolated nodal recurrence is uncommon (≤ 5%) therefore observe the neck.

- Patients with a residual nodal mass in the neck have a ~30-40% risk of having pathologically positive residual disease (non-HPV oropharyngeal cancer).

- Post radiotherapy biopsy of the residual neck mass is unreliable to guide the need for neck dissection.

- Therefore perform neck dissection in patients with residual nodal abnormality.

- Some advocate for ND in all patients presenting with nodal disease regardless of response (planned neck dissection).
More selective approach to choosing patients for neck dissection would be advantageous
Improving the predictive value of post-therapy imaging for residual nodal disease through functional imaging (FDG PET-CT)
Utility of PET for the detection of residual neck nodes after radiotherapy in Head and Neck cancer

- 39 patients with node positive HNC who had a complete response at the primary site and a residual neck mass on CT after radiotherapy

- PET performed 12 weeks post therapy

- 32 pts with a residual neck mass were PET negative in the neck
  - 5 neck dissection - all pathologically negative
  - 27 patients observed with one neck failure
  - Negative Predictive value 97%

- 7 patients were PET positive in the neck
  - all had a neck dissection
  - Positive Predictive value 71%

Porceddu S et al Head Neck 2005
Utility of PET for the detection of residual neck nodes after radiotherapy in Head and neck cancer

- 39 patients with node positive HNC who had a complete response at the primary site and a residual neck mass on CT after radiotherapy
- PET performed 12 weeks post therapy
- 32 pts with a residual neck mass were PET negative in the neck
  - 5 neck dissection - all pathologically negative
  - 27 patients observed with one neck failure
  - Negative Predictive value 97%
- 7 patients were PET positive in the neck
  - all had a neck dissection
  - Positive Predictive value 71%

Porceddu S et al Head Neck 2005
Prospective study of PET-directed management of the neck in node positive (N+) head and neck cancer following definitive radiotherapy with or without systemic therapy

Purpose

• Can PET predict who could safely have the neck observed despite the presence of any residual nodal CT abnormality in patients who achieved a complete response at the primary site
Endpoint

- Assess the isolated nodal failure rate in patients who achieve a complete response at the primary site
PET-guided policy of the neck

Mucosal N+ HNSCC treated with RT+/-Chemo
Complete response at primary site
12 week re-staging FDG-PET/CT
Synchronous diagnostic CT scan

- PET
  - Neck Negative Observed
  - Neck Equivocal
    - Repeat 4-6 weeks
  - Neck Positive
    - Neck dissection

^ Regardless of any residual nodal abnormality on re-staging CT scan
Outcomes

123 patients treated during the study period (Jan05- Apr 09)

112 (91%) patients achieved a complete response at the primary site by 12 weeks

Oropharyngeal 83 (74%)
p16+ 59 (53%)

Median FU 28 (12-60) months
Outcomes in the neck

<table>
<thead>
<tr>
<th>12 week nodal response</th>
<th>Patient No. n=112</th>
<th>Post-therapy treatment</th>
<th>Outcome (median FU 28m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT no residual PET Negative</td>
<td>62 (55%)</td>
<td>Observed</td>
<td>Isolated nodal failures = 0</td>
</tr>
<tr>
<td>CT Residual PET Negative</td>
<td>41 (37%)</td>
<td>Observed</td>
<td>Isolated nodal failures = 0</td>
</tr>
<tr>
<td>CT Residual PET Positive</td>
<td>9 (8%)</td>
<td>8 ND (7%)</td>
<td>Isolated nodal failures = 3 (2.7%)</td>
</tr>
</tbody>
</table>

^ Residual node defined as abnormality >10mm or necrotic of any size on CT
# Outcomes in the neck

<table>
<thead>
<tr>
<th>12 week nodal response</th>
<th>Patient No. n=112</th>
<th>Post-therapy treatment</th>
<th>Outcome (median FU 28m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT no residual PET Negative</td>
<td>62 (55%)</td>
<td>Observed</td>
<td>Isolated nodal failures = 0</td>
</tr>
<tr>
<td>CT Residual PET Negative</td>
<td>41 (37%)</td>
<td>Observed</td>
<td>Isolated nodal failures = 0</td>
</tr>
<tr>
<td>CT Residual PET Positive</td>
<td>9 (8%)</td>
<td>8 ND (7%)</td>
<td>Isolated nodal failures = 3 (2.7%)</td>
</tr>
</tbody>
</table>

^ Residual node defined as abnormality >10mm or necrotic of any size on CT
## Outcomes in the neck

<table>
<thead>
<tr>
<th>12 week nodal response</th>
<th>Patient No. n=112</th>
<th>Post-therapy treatment</th>
<th>Outcome (median FU 28m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT no residual PET Negative</td>
<td>62 (55%)</td>
<td>Observed</td>
<td>Isolated nodal failures = 0</td>
</tr>
<tr>
<td>CT Residual PET Negative</td>
<td>41 (37%)</td>
<td>Observed</td>
<td>Isolated nodal failures = 0</td>
</tr>
<tr>
<td>CT Residual PET Positive</td>
<td>9 (8%)</td>
<td>8 ND (7%)</td>
<td>Isolated nodal failures = 3 (2.7%)</td>
</tr>
</tbody>
</table>

^ Residual node defined as abnormality >10mm or necrotic of any size on CT
Outcomes in the neck

12 week nodal response | Patient No. n=112 | Post-therapy treatment | Outcome (median FU 28m)
--- | --- | --- | ---
CT no residual PET Negative | 62 (55%) | Observed | Isolated nodal failures = 0
CT Residual PET Negative | 41 (37%) | Observed | Isolated nodal failures = 0
CT Residual PET Positive | 9 (8%) | 8 ND (7%) 1 palliative 6/8 true positive | Isolated nodal failures = 3 (2.7%)

^ Residual node defined as abnormality >10mm or necrotic of any size on CT
Utility of PET for the detection of disease in patients with a residual structural nodal abnormality following radio(chemo)therapy in node positive head and neck cancer

- Negative Predictive Value = 98%
- Positive Predictive Value = 78%

Porceddu S et al Head Neck 2011
Conclusion

- PET-guided policy of the neck in node positive HNSCC following a complete response at the primary site results in a very low isolated nodal failure rate following definitive RT.

- This policy appropriately spares a neck dissection in patients who are PET negative regardless of the presence of a residual CT nodal abnormality.
T1N2bM0 oropharyngeal SCC

Pre-therapy
12 weeks
12 months
# Impact of PET on neck dissection rate

<table>
<thead>
<tr>
<th>Neck Dissection Policy</th>
<th>Neck Dissection rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Planned Surgery for N2-3 (excluding N1)</td>
<td>101 (90%)</td>
</tr>
<tr>
<td>Neck surgery for residual CT abnormality (&gt;10mm or necrotic)</td>
<td>50 (45%)</td>
</tr>
<tr>
<td>PET-directed Policy</td>
<td>8 (7%)</td>
</tr>
<tr>
<td>For an isolated nodal failure rate of 2.7% (FU 28mths)</td>
<td></td>
</tr>
</tbody>
</table>

Median FU 62 months total nodal failures 4%  
Sjovall J et al Oral Oncology 2015
Economic analysis of FDG-PET–guided management of the neck after primary chemoradiotherapy for node-positive head and neck squamous cell carcinoma

David I. Pryor, MBBS, FRANZCR, Sandro V. Porceddu, MBBS, MD, FRANZCR, Paul A. Scuffham, BA, PhD, Jennifer A. Whitty, BPharm, PhD, Paul A. Thomas, BMed, FRACP, Bryan H. Burmeister, MBChB, MD, FRANZCR

1Division of Cancer Services, Princess Alexandra Hospital, Brisbane, Australia, 2School of Medicine, Faculty of Health Sciences, University of Queensland, Brisbane, Australia, 3Centre for Applied Health Economics, School of Medicine, Griffith Health Institute, Griffith University, Brisbane, Australia, 4Queensland PET Service, Royal Brisbane and Women's Hospital, Brisbane, Australia.
PET-CT Surveillance versus Neck Dissection in Advanced Head and Neck Cancer

PET-Neck Trial schema

Eligible and consenting patient

- PET-CT guided ‘active surveillance’
- Randomised 1:1
  - Stratified by:
    - Centre
    - T stage (T1-T2, T3-T4)
    - N stage (N2a-N2b, N2c-N3)
    - Disease site
    - Chemotherapy schedule
    - Timing of neck dissection (before or after CRT)
- Standard treatment ‘planned ND’
  - CRT
  - ND before or after CRT

PET-CT & Assessment 9-13 weeks after CRT completion

If CR primary: is neck +ve or equivocal on PET-CT?
- Yes: Neck dissection within 4 weeks
- No

Clinical Follow up:
Year 1 - monthly; Year 2 - two monthly
Overall survival (Primary Endpoint)

Number at risk
Neck dissection  282  243  204  118  32  8
PET-CT surveillance  282  259  224  110  33  6
<table>
<thead>
<tr>
<th></th>
<th>Neck dissection arm</th>
<th>Surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intended pre CRT</td>
<td>Intended post CRT</td>
</tr>
<tr>
<td>Total</td>
<td>77</td>
<td>205</td>
</tr>
<tr>
<td>2-year loco-regional control</td>
<td>94.8%</td>
<td>92.0%</td>
</tr>
<tr>
<td>2-year recurrence-free</td>
<td>85.7%</td>
<td>83.5%</td>
</tr>
<tr>
<td>Nodal recurrence</td>
<td>0.7%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Node only recurrence</td>
<td>0.4%</td>
<td>1.1%</td>
</tr>
</tbody>
</table>
Validation of the ICON-S staging for HPV-associated oropharyngeal carcinoma using a pre-defined treatment policy

Sandro V Porceddu a,b,* Rob Milne b Elizabeth Brown a,c Anne Bernard d Reza Rahbarg a Bena Cartmill a Matthew Foote a,b Margaret McGrath a Jermaine Coward a,b Benedict Panizza b,e

Kaplan-Meier estimates of overall survival by ICON-S stage (in years)

Overall survival (%)

1.0
0.8
0.6
0.4
0.2
0.0

Time (years)

n=279

Number at risk

Stage 1 143 138 104 50 10 –
Stage 2 82 75 47 26 12 –
Stage 3 66 57 37 16 6 2
Recommended guidelines for risk-adapted management of node positive HNSCC post-RT

- Definitive RT N+HNSCC
  - 6 week clinical evaluation
    - Primary and/or nodal progression
      - Primary and nodal regression
        - 12 week complete response at primary site clinical and PET/CT evaluation of the neck
          - PET-/CT+
            - High risk*
              - 2 to 3 monthly clinical and imaging observationΔ
            - Low risk*
          - PET-/CT+
            - Observation
          - PET/CT negative
            - PET/CT negative
              - 4 to 6 weeks repeat PET/CT
            - PET/CT positive or equivocal PET/CT
              - Persistent equivocal or positive PET findings
                - Progressive nodal disease
                  - Salvage surgery
  - PET+/CT+
    - Equivocal PET/CT
Acknowledgements

**Radiation Oncology**
Bryan Burmeister  
Matthew Foote  
Elizabeth Brown  
Bena Cartmill  
David Pryor  
Ben Chua

**Medical Oncology**
Margie McGrath  
Jim Coward

**ENT Surgery**
Ben Panizza  
Chris Perry  
Scott Coman  
James Bowman  
Ben Wallwork  
Raefe Gunderlach

**Data Manager/Statistics**
Anne Bernard  
Josephine Logan

**Diagnostic Imaging**
PAH  
RBWH

**Radiation Oncology Fellow**
Howard Liu