From ICARO 1 to ICARO 2: The Radiation Oncologist Perspective

Eduardo Rosenblatt
ICARO2, Vienna, 20/06/2017
Radiotherapy in the broader context

- RT is a fundamental component of effective cancer treatment for cure and palliation
- It has been established that at least 50% of cancer patients would benefit from RT
- Virtually absent from global health discourse
- Receives limited domestic and international funding

Rosenblatt et al. 2015
Atun et al. LO 2015
ASR cancer incidence and mortality rates/100.000 between 1975-2012

Incidence rates tend to increase

A substantive decline in ASR mortality

WHO/IARC, World Cancer Report, 2014
10-year relative survival in adults in England/Wales, 1971-2007

Myeloma
Stomach
Oesophagus
Brain
Lung
Pancreas
International Conference on Advances in Radiation Oncology

ICARO 1 (April 2009)  ICARO 2 (June 2017)
The historical development of radiotherapy...

has been the search for strategies to enhance the therapeutic ratio of radiation as a cancer treatment:

- FRACTIONATION
- HYPERTHERMIA
- RADIOSENSITIZERS
- RADIOPROTECTORS
- OXYGEN
- CHEMO-RADIATION
- TARGETED THERAPY
- 3D CONFORMALITY
- IMRT/IGRT
- PARTICLE THERAPY

Stanford, 1957
Advances in Radiation Oncology

Closer approximation of the treatment volume to the defined target

Biological means to increase the differential response between tumor and normal tissues/structures

Clinical trials to provide evidence of the superiority of new strategies
Significant developments in RO over the past decade:

• Imaging
• Computer and information technology
• Molecular and clinical radiobiology
• Treatment planning
• Delivery of RT
• Combined modality treatment
• Dosimetry of small fields
• Multidisciplinary decision-making
• Supportive and palliative care
Debate 1
Cobalt-60 – is it time for retirement?

ICARO-1
- There remains a role for Co-60 teletherapy in LMICs.
- New technical developments allow the implementation of highly conformal treatment techniques, but this increases the costs to the level of linear accelerators.

ICARO-2
<table>
<thead>
<tr>
<th>Equipment type</th>
<th>Count</th>
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<tbody>
<tr>
<td>Linacs</td>
<td>11.444</td>
</tr>
<tr>
<td>Radionuclideide</td>
<td>2.185</td>
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<tr>
<td>Total megavoltage</td>
<td>13.629</td>
</tr>
<tr>
<td>Co-60</td>
<td>16%</td>
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</table>
Debate 2
IMRT – are you ready for it?

ICARO-1
• Robust clinical trials are necessary to demonstrate the benefits of new technologies before they are adopted into widespread use

• A new and unproven technology should not be universally adopted as a replacement for established proven technologies

ICARO-2
Should IMRT be the standard of care?

Debate
THURSDAY 22
12:00 – 13:00

YES NO
Debate 3
Do we need proton therapy?

ICARO-1
• Physical dose-distributions are superior to those of photons
• The cost of establishing and maintaining facilities is significant
• Clinical trials are underway
• Whether the clinical gains from proton therapy will outweigh the costs is an unresolved issue ...

ICARO-2

<table>
<thead>
<tr>
<th>Operational facilities</th>
<th>73</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protons</td>
<td>63</td>
</tr>
<tr>
<td>Carbon-ion</td>
<td>11</td>
</tr>
</tbody>
</table>

| Facilities under construction | 41 |
| Facilities in planning        | 20 |
Imaging and functional molecular imaging - IGRT

CT- (green) and PET/CT (red) defined PTVs in the same patient.
Mac Manus et al. 2013

MR-linac
(Royal Marsden Hospital, UK)

2004
J.F. Dempsey (Univ. of Florida)
J.J. Lagendijk, W. Raaymakers
(Utrecht, Netherlands)
P.J. Krall, M. Barton (Sydney, Australia)
G. Fallone (Univ. of Alberta, Canada)
Volumetric Arc IMRT
Stereotactic techniques

STEREOTACTIC RADIOThERAPY

• 3D imaging
• Precise positioning and immobilization
• Highly focused beams that converge in a defined volume
• IGRT

SBRT

• Early stage NSCLC
• Liver
• Spine
• Prostate
• Radical treatment of oligometastasis

• ASTRO-ACR/AAPM/IAEA
Hypofractionation

ICARO 1
• Patient convenience
• Reduced Tx time
• Saving resources
• Feasible with highly conformal (precision) RT

ICARO 2
• Prostate
• Breast
  – Whole breast
  – APBI
• Oligo-

“Trials change practice --- slowly!”

Søren Bentzen, J. Yarnold

20.06.2017 Rosenblatt ICARO2
ASTRO Choosing Wisely® (2013)

• Don’t initiate whole breast radiotherapy as a part of breast conservation therapy in women age ≥50 with early stage invasive breast cancer without considering shorter treatment schedules.
• Don’t initiate management of low-risk prostate cancer without discussing active surveillance.
• Don’t routinely use extended fractionation schemes (>10 fractions) for palliation of bone metastases.
• Don’t routinely recommend proton beam therapy for prostate cancer outside of a prospective clinical trial or registry.
• Don’t routinely use IMRT to deliver whole breast radiotherapy as part of breast conservation therapy.
an inconvenient truth
(for radiation oncologists)

The manual contouring of targets and OAR has become a bottle-neck in the overall process of radiotherapy
Automation in contouring and planning

**AUTO-CONTOURING**

- Saves time
- Reduces inter-observer variation

**AUTOMATED RT PLANNING**

**AUTOMATED QA**

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Brachytherapy

ICARO1

- Brachytherapy session
- Lunch symposium on Co-60 BT

ICARO2

- HDR firmly established
- Co-60 HDR also popular
- Image-guided BT planning
- New afterloading devices
- Hybrid applicators
- Electronic BT
- Robotic BT (for prostate seed)
- Y-90 microspheres
- Improvements in in-vivo dosimetry
- GEC-ESTRO recommendations
- ICRU Report 89

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“Radiation offers new cures, and ways to do harm”

Radiotherapy accidents associated with the new technologies ... prompted review and strengthening of radiation protection issues

- Regulations
- Staffing
- Training
- Incident reporting
- Radiation safety
Biology and Radiobiology

- Molecular targeted therapy
- Angiogenesis and anti-angiogenesis agents
- Paracrine signalling
- Stem cell therapeutics
- Nanotechnology
- Tumour microenvironment
- Radiogenomics
- Radiobiology of single ablative doses
- Radiobiology of particle therapy
Molecular Targeted Therapy

2-yr Loco regional control

Overall Survival

41 vs. 50%
HR 0.68 (0.52–0.87) P=0.005

45 vs. 55%
HR 0.74 (0.57–0.97) P=0.03

J. Bonner et al. NEJM 2006
Radiotherapy and Immunotherapy; a paradigm shift?

• Radiation induces immune modulation
• RT alone does not have the intensity to generate enough immune signals...
• Therefore, a partnership of radiation with targeted immunotherapy agents appears to be important

Personalized radiotherapy

PERSONALIZED MEDICINE

PERSONALIZED RADIOTHERAPY

• Clinical
• Stage
• Histopathologic
• Tumour shape
• Radiogenomics

One-size-fits-all vs. Biological adaptation

2009 RADIogenomics CONSORTIUM
Radiation Oncology and Global Cancer Challenges

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>UNIATF</td>
<td>UN Interagency Task Force for NCDs</td>
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<tr>
<td>GTFRTCC</td>
<td>Global Task Force for RT in Ca. Control</td>
</tr>
<tr>
<td>ESTRO-GIRO</td>
<td>Global Impact of Radiation in Oncology</td>
</tr>
<tr>
<td>PACT-AGART</td>
<td>Advisory Group on Access to RT</td>
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<tr>
<td>NCI-CGH</td>
<td>NCI Center for Global Health</td>
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<tr>
<td>ICEC</td>
<td>International Cancer Expert Corps</td>
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<tr>
<td>ICCP</td>
<td>International Cancer Control Partnership</td>
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Conclusions:

1. The 8 years between ICARO1-ICARO2 have accompanied a decade of rapid development in the field of radiation oncology in its technical, clinical, biological and translational research branches.

2. There is increased awareness and action to address global disparities in access to radiotherapy services.

3. The IAEA-ICARO meetings represent a step in this direction.