How effective is current clinical trial QA

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Contents

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• Implementation of clinical trial QA
• Defining standards and assessment against a benchmark
• How well are we doing?
• The future
Key QA process areas

- Imaging Target volume & OAR Outlining
- Treatment planning and optimisation
- Treatment delivery and verification
- Dosimetry audit
QA processes

Central independent QA is acknowledged as essential for current radiotherapy clinical trials

• **Baseline**
  • Ensures centres have the equipment, expertise and ability to comply with trial protocol requirements

• **Pre accrual**
  • Confirms centres are able to deliver treatment accurately and consistently according to specific trial guidelines

• **During accrual**
  • Assures continued compliance and consistency of treatment delivery both within individual centres and across all recruiting centres throughout the trial
Implementation of clinical trial QA

- RT guidelines
- Workshops
- TMG Meetings

Baseline:
- Facility Questionnaire
- Beam Output Audit

Pre-Accrual:
- Dummy Run
- Benchmark Case
- Outlining
- Planning
- Complex Treatment Dosimetry Check
- Virtual Phantom Procedure

During Accrual:
- Individual Case Review
  - Prospective
  - Retrospective
- Review of Treatment Records
- Protocol Compliance & Dosimetry Site Visit

Advice and Support
Defining standards
RT Guidelines and FQ

- RT guidelines
  - Comprehensive document
  - Treatment planning and delivery

- FQ
  - Demographics, workload, equipment and procedures
  - Align with the RT guidelines
  - Adherence to protocol requirements
Defining standards
Target volume and OAR outlining

• Progression of outlining process through trials

• Creation of a reference set of contours “gold standard”
  • Created by an expert individual
  • Created through the consensus agreement of a panel of experts

• Consensus standard
  • single contour
  • contour “cloud”

Benchmark case
Individual gold standard

Benchmark case
Consensus gold standard

Outlining atlas

National standards

International standards
Defining standards
Planning and optimisation

- Prioritisation of planning objectives
  - Target volume and OARs

- Provision of dose volume constraints
  - Mandatory
  - Optimal

<table>
<thead>
<tr>
<th>Dose Constraints</th>
<th>Optimal</th>
<th>Mandatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTV $D_{95%}$</td>
<td>$\geq 95%$ of prescribed dose</td>
<td>$\pm 2%$ of prescribed dose</td>
</tr>
<tr>
<td>CTV MeanDose</td>
<td>$\pm 1%$ of prescribed dose</td>
<td>$\pm 2%$ of prescribed dose</td>
</tr>
<tr>
<td>PTV $D_{95%}$</td>
<td>$\geq 90%$ of prescribed dose</td>
<td></td>
</tr>
<tr>
<td>PTV $D_{95%}$</td>
<td>$\geq 90%$ of prescribed dose</td>
<td>$\geq 85%$ of prescribed dose</td>
</tr>
<tr>
<td>PTV $D_{1cc}$</td>
<td></td>
<td>$\leq 107%$ of prescribed dose</td>
</tr>
</tbody>
</table>
## Assessment against a benchmark

<table>
<thead>
<tr>
<th>Benchmark case</th>
<th>Dummy run</th>
</tr>
</thead>
</table>
| Trial selected and generated case  
Planning and/or delineation on a common CT dataset                               | In-house patient  
Protocol compliance treatment plan  
Simple connectivity check                                                       |
| Objective assessment against a pre-defined set of reference contours or plan    | More subjective assessment no reference contours or plan                   |
| Direct comparison across all submissions                                       | No comparison across submissions                                           |
|                                                                                | Patient selection according to trial eligibility criteria                  |
Assessment against a benchmark

• Review performance against trial standards
  • Conformity metrics
  • Pre-defined dose-volume constraints

• Highlight potential protocol variations

• Pre-accrual QA feedback
  • increases the likelihood that trial patients are treated according to protocol
Individual case review (ICR)

• Review of the actual treatment plan and delineation of trial patients
  • Retrospective: after treatment completion
  • *Timely retrospective: during treatment*
  • Prospective: before treatment starts

• Prospective/real time independent central evaluation
  • Increasing demand
  • Allows correction of potential protocol variations
  • Short turnaround time
  • Avoid treatment delays
  • Potentially resource intensive
Verification of treatment delivery

• Dosimetry check
  • Virtual phantom: in-house phantom.
  • Complex treatment dosimetry check: phantom provided by the QA group/approved audit group
    • Postal
    • Site visit

• Image guidance
  • Adaptive and plan of the day (POD)
  • QA approaches
    • Equipment/software
    • Plan selection competency and compliance
So how well are we doing........?
Target volume outlining SCOPE1 (oesophagus)

- Comparison against a gold standard GTV
- Median JCI 0.69 (interquartile range, 0.62-0.70)
- Local conformity index (L-CI) established
  - Highlighted greatest GTV discordance on individual CT slices

Gwynne et al. IJROBP. 2012;84(4):1037-1042
Target volume and OAR outlining
ART-DECO (head and neck)

- Evaluated degree of inter-observer variability
- Impact of QA feedback on standardising outlining
- Improvement following QA Review and subsequent submissions

Slide courtesy of Dr John Conibear
Planning and optimisation
De-ESCALETaTE (head and neck)

- QA process improves RT plan quality
- 63% of submissions required at least 1 re-submission for protocol compliance
- Statistically significant difference to target volume coverage

Planning and optimisation
National UK SABR programme

• Spillage” of prescription dose

• Improvement in dose conformity
Pre-acrual QA CONVERT (lung)

- Is pre-acrual QA effective?
- Comparison of the pre-acrual QA results with during accrual QA
- Pre accrual QA improved protocol compliance and reduced deviations in recruited patients

<table>
<thead>
<tr>
<th>Category</th>
<th>Pre-acrual</th>
<th>During Accrual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligibility criteria</td>
<td>4 deviations</td>
<td>All compliant</td>
</tr>
<tr>
<td>Beam energy</td>
<td>3 deviations</td>
<td>All compliant</td>
</tr>
<tr>
<td>Eligibility criteria</td>
<td>4 deviations</td>
<td>All compliant</td>
</tr>
<tr>
<td>GTV outlining</td>
<td>6 deviations</td>
<td>6 deviations</td>
</tr>
<tr>
<td>OAR doses constraints</td>
<td>All compliant</td>
<td>All compliant</td>
</tr>
<tr>
<td>Planning technique</td>
<td>13 deviations</td>
<td>1 deviation</td>
</tr>
</tbody>
</table>
During accrual QA (ICR)
SCALOP (Pancreas)

• Evaluated the feasibility of a plan assessment form (PAF) as a tool for during accrual QA

• Excellent correlation between PAF and electronic dose data

• PAF can be a simple and effective tool to evaluate real-time RT compliance

Nixon et al. IJROBP, 2013;87(S2):S306
Protocol compliance

FAST FORWARD (breast)

• Analysed 3600 plans to confirm protocol compliance
• 3.4% of data not achieving one or more of the protocol dose objectives
• Only 1.5% were avoidable variations from the protocol dose objectives

Protocol dose objectives:
- PTV V95% ≥ 90%
- PTV V105% ≤ 7%
- PTV V107% ≤ 2%
- D_{max} ≤ 110%
- Ipsilateral lung V30% ≤ 17%
- Heart V25% ≤ 5% and V5% ≤ 30%

Zotova et al. Radiother. Oncol. 2015;115(S1):S209
Dosimetry audit

Identify outliers
Achieve consistent across all centres

CH. Clark et al. Radiother Oncol. 2014;113(2):272–278
J. Lee et al. Radiother Oncol. 2015;115(S1):S74-S75
P. Diez et al. Radiother Oncol. 2015; 115(S1): S139
• Remote training and assessment programme
• IGRT competence and protocol interpretation
  • Decision making
  • Accurate image
  • Plan selection
• Site visit
• Prepared participants for POD selection

Callender et al. Radiother. Oncol. 2015;115(S1):S209
The future

How effective is current clinical trial QA?

Improved quality of the radiation technique
Increased protocol compliance

Continual advances in technology
Increased trial participation
Rarer tumour sites
Continual evolution of QA activities

Translation into improved robustness of study results?

Streamlined efficient approach to QA?
Acknowledgements

National RTTQA group members
Investigator sites
Individual trial programmes
Collaborating groups and organisations