Guidelines for the use of inversely planned treatment techniques in Clinical Trials: IMRT, VMAT, TomoTherapy

VERSION 2.1
April 2015
### Abbreviations & Glossary

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>CQMS</td>
<td>Central Quality Management System</td>
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<tr>
<td>IMRT</td>
<td>Intensity Modulated Radiation Therapy; here using static gantry</td>
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<tr>
<td>VMAT</td>
<td>Volumetric Modulated Arc Therapy</td>
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<td>IGRT</td>
<td>Image Guided Radiation Therapy</td>
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<td>QA</td>
<td>Quality Assurance</td>
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<td>TMC</td>
<td>Trial Management Committee</td>
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<td>3D CRT</td>
<td>Three-dimensional Conformal Radiation Therapy</td>
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<td>CT</td>
<td>Computerised Tomography</td>
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<td>MLC</td>
<td>Multi Leaf Collimator</td>
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<td>RANZCR</td>
<td>Royal Australian and New Zealand College of Radiologists</td>
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<td>ACDS</td>
<td>Australian Clinical Dosimetry Service</td>
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<td>TROG COO</td>
<td>TROG Central Operations Office</td>
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Executive Summary

Inversely planned treatment techniques, including IMRT, VMAT and Tomotherapy, have become increasingly the standard of care since the first issue of TROG guidelines. This review aims to update requirements for trials participation to ensure robustness of delivered dose across participating centres, to support staff at participating centres, and to enhance trials accrual.

The uses of inversely planned techniques in trials fall into three categories:

1. No RT question, or RT dose not critical
2. RT is part of the study question, but IMRT is not considered likely to impact on the study question.
3. Inversely planned treatments form all or part of the study question; or the study cannot be conducted without inversely planned treatments.

All centres will be asked to provide:

a. Facility questionnaire, in two parts: TROG QA has prepared a generic questionnaire, with results held on the website; a short, additional trial-specific IMRT questionnaire.

b. Benchmarking exercise for the trial: for a provided CT dataset, preparation and submission of treatment plan using CQMS.

c. Dosimetric quality assurance exercise, with requirements depending on the category of the trial question.

TROG QA staff are happy to advise centres and discuss any practical issues. Please contact qa@trog.com.au.

These guidelines have been prepared by TROG QA New Technologies and Techniques Committee and approved by TROG Scientific Committee. Version 2.0 replaces the guidelines issued in September 2008 and revised in October 2009.
1. Inversely planned treatments in TROG Clinical Trials

1.1 Scope

These guidelines cover the following treatment delivery techniques:

- IMRT, ie static gantry IMRT, using either step and shoot MLC fields, or dynamic MLC fields.
- VMAT, ie dynamic gantry IMRT. Manufacturers’ trade names are Varian RapidArc [1]; Elekta VMAT [2].
- TomoTherapy with HiArt planning system [3].

Forward planned “field-in-field” techniques are subject to 3D conformal treatment guidelines.

IGRT requirements are trial-specific and are not part of this document.

The TROG protocol template refers to these guidelines, which are specifically applicable to current trials introducing inversely planned techniques as a treatment option and to trials under development when QA procedures are being developed.

1.2 Introduction

Static gantry IMRT has been shown to improve outcomes [4] and longer term toxicity [5, 6] in prostate treatments compared with previous techniques. The TROG project Assessment of New Radiation Oncology Techniques and Technologies (ANROTAT) concluded that “IMRT has been shown to be both more effective and less costly than its comparator three-dimensional conformal radiation therapy (3DCRT) in three disease sites: naso-pharynx, post-prostatectomy and anal canal” [7]. RANZCR have reported that “Dynamic gantry inversely planned treatment (VMAT) provides significant evidence that volumetric modulated arc therapy, when performed with multiple arcs, achieves superior target dose homogeneity and adjacent normal tissue sparing in a range of tumour sites when compared to 6 field 3D conformal radiotherapy” [8]. It is evident that these techniques are being generally adopted in routine clinical practice and becoming the standard of care.
The challenge for clinical trials groups is to incorporate these new techniques into currently open trials, and developing trials, while maintaining robustness and validity of delivered dose data. Clinical dose reporting follows ICRU recommendations [9]. US and UK trials groups have published guidelines with IMRT credentialling requirements [10, 11] and details of VMAT audits [12, 13].

The ANROTAT project included dosimetric site visits with phantoms, with protocols and tolerances developed by a committee of experienced medical physicists. This experience has enhanced the development and update of the TROG guidelines, which aim to ensure robustness of delivered dose across participating centres, to support staff at participating centres, and to enhance trials accrual.

2. Credentialling of inversely planned treatments

2.1 Facility questionnaire

TROG QA have centralised the generic part of the facility questionnaire, with information on equipment and facilities being held on CQMS, and covering 3D conformal treatments. The facility questionnaire requires centres to submit details of their local patient-specific and machine-specific QA practices. Additional technical aspects will be covered by trial-specific short questionnaires, eg IMRT in TROG 08.08 TOPGEAR. Information will be held centrally, and with the centre’s permission, may be made available for other trials.

The TROG 08.08 TOPGEAR IMRT module asks for information on treatment planning system algorithms; treatment unit and MLC performance; IGRT techniques used; patient immobilisation; patient-specific QA procedures and dose verification; and participation in external IMRT audits.

2.2 Trial-specific Benchmarking exercise

The trial QA process will include benchmarking exercises, to ensure the centre’s ability to comply with the trial protocol and the QA review process.

The benchmarking exercise will include a contouring and planning exercise with external review by independent reviewers (appointed by the TMC) using TROG plan review software including MIM [14] or SWAN [15]

Contouring of targets and normal tissue is critical for all complex volumes/plans required in inverse planning, and especially for uncommon sites/primaries, and can be the weakest link in the treatment delivery chain. The external review of the contours is fundamental to the validity of the treatment plan.
2.3 Dosimetric Quality Assurance

2.3.1. All centres will be asked to provide evidence, by report, of an external level 1 audit by a recognised body, such as Australian Clinical Dosimetry Service (ACDS), within the last 2 years. Reports from other bodies may be submitted to TROG QA office for consideration.

2.3.2. Clinical trial data robustness relies on the equivalence of delivered dose in each participating centre. Traditionally this has been validated by a level 3 dosimetric audit site visit by a trial representative, using the same phantom and equipment at each centre. It has been the responsibility of each trial to cover the QA procedures as required. In some instances, it has been possible for other trials to accept credentialling reports. TROG QA regards the validity of the level 3 audit report ideally as up to 5 years, and will discuss any issues with individual centres.

2.3.3. Due to limited resources, it is not always possible to make the credentialling site visits. TROG is working on alternative approaches, which would enable efficient timescales for the credentialling process.

2.3.4. Some centres are satellite centres to a principal centre, or part of a network, and may be considered in conjunction with the principal centre on a case-by-case basis, provided that:

- Equipment is the same: manufacturer, matched linacs, treatment planning system and beam models, oncology information management system
- Common QA protocols across centres
- Staff rotate across centres.

Each geographical centre is required to provide a level 1 audit report as in 2.3.1. TROG QA will discuss the position with centres.

2.3.5. International centres wishing to take part in TROG trials are invited to submit evidence of dosimetry audits, from recognised bodies, to TROG QA for consideration.

2.3.6. All centres using TomoTherapy shall have an external dosimetry audit to assess the delivered dose and ensure consistency of delivered dose for comparison with linear accelerator
treatment deliveries. TomoTherapy treatments have been introduced in Australia since 2011, and as such are a new technique which TROG must validate.

2.3.7. VMAT, ie dynamic gantry modulated delivery with inverse planning, is regarded as a new technique and each centre wishing to use VMAT in TROG trials must have an external dosimetry audit. There are differences in planning and delivery techniques between the manufacturers, eg in gantry and dose modulation prioritising. The external audit is therefore only valid for the specified equipment.

2.3.8. Other new treatment delivery techniques, including Cyberknife, will require the centre to have an external dosimetry audit – contact TROG QA for advice.

2.3.9. Each trial will set the tolerance criteria for acceptance, for both point dose accuracy and gamma analysis of measured dose planes [16, 17].

2.3.10. The uses of inversely planned techniques in trials fall into three categories with increasing levels of QA requirements:

A. No RT question, or RT dose not critical, or <20% of prescription dose delivered using inversely planned techniques

TROG minimum requirements:

- Facility questionnaire detailing IMRT delivery and QA procedures, fulfilling tolerance criteria specified by the Trial Management Committee and TROG QA.

B. RT is standard in both arms

TROG minimum requirements:

- Facility questionnaire detailing IMRT delivery and QA procedures.

- Evidence of relevant and appropriate IMRT level 3 dosimetric audit by recognised body OR evidence of activities and data that provides a similar level of confidence in the delivery process as a level 3 audit. This could be a remote process. Details to be discussed with the TMC and TROG QA.
• Centres using VMAT, TomoTherapy or other new techniques will require an external dosimetry audit (see 2.3.5 to 2.3.7 above).

C. RT is the research question, specifically the technology/technique being tested

TROG minimum requirements:

• Evidence of relevant and appropriate IMRT level 3 dosimetric audit by recognised body.

• All patients treated with IMRT, VMAT or Tomo must have individual plan QA.

• Dosimetric audit site visit by TMC/TROG may be required, as specified by the TMC physicist and radiation therapist.

• Centres using VMAT, TomoTherapy or other new techniques will require an external dosimetry audit (see 2.3.5 to 2.3.7 above).
## 3. Information for trial investigators

TROG QA are anxious to support trial investigators, for current trials introducing inversely planned techniques, and for trials under development when QA procedures are being developed. This checklist is intended to support investigators.

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<tr>
<th>Area</th>
<th>Comments</th>
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<tbody>
<tr>
<td>TROG protocol template</td>
<td>The protocol template covers all areas to be addressed, and is available from TROG QA</td>
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<tr>
<td>Multi-professional trial QA team</td>
<td>Each team member should have good clinical experience using the inversely planned technique. The team may be drawn from different centres and cover all professional disciplines.</td>
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<tr>
<td>QA programme [to assess compliance with trial protocol]</td>
<td>Contact TROG QA office for advice and information on requirements and documentation specific to the trial, including facility questionnaire and benchmarking case.</td>
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<td></td>
<td>Discuss QA requirements including dose-volume constraints and definitions of minor/major violations.</td>
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<tr>
<td>Centre credentialling requirements</td>
<td>Contact TROG QA office to discuss the category of credentialling required, and any previous audits which may be relevant for this trial</td>
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<tr>
<td>Notification to centres: current trials only</td>
<td>Inform centres of specific requirements, eg external dosimetry audit for new technique</td>
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<tr>
<td>Additional requirements</td>
<td>Specify any requirements, eg IGRT</td>
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4. References


3. The TomoTherapy Hi·Art treatment system uses a patented multileaf collimator to modulate the intensity of the radiation beam 2013 26 Nov 2013]; Available from: http://www.tomotherapy.com/.


11. RTTQA. RTTQA IMRT credentialing program. 27 Nov 2013]; Available from: http://www.rttquality.org.uk/.


Acknowledgements

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