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Radiation therapy quality assurance in clinical trials – Global harmonisation group

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Participation in large multi-centre clinical trials aids establishment of the safety and efficacy of new cancer treatments and methods. Oncology clinical trials have contributed to improved local control, overall survival and quality of life for patients with varying disease types [1]. Radiation Therapy is indicated in the course of treatment for more than 50% of all cancer patients [2,3] and consequently a high percentage of oncology clinical trials include radiotherapy within their treatment schema.

Collaboration between global clinical trial groups and organisations has increased the number of patient records available for analysis permitting faster recruitment [4], broader acceptance and wider impact of trial results. Global cooperation is also essential in the environment of rare cancers [5], in order to be able to create sufficiently large patient data sets within a reasonable recruitment period. A successful example is the EORTC 26981/ National Cancer Institute of Canada (NCIC) CE3 intergroup trial, where 573 Glioblastoma

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patients were randomised within 20 months [6], despite the low prevalence of the disease among the general population.

Globally, clinical trial groups and organisations have independently implemented their own Radiation Therapy (RT) Quality Assurance (QA) programs within their corresponding large multicentre clinical trials. Various trial groups have reported that the implementation of RTQA procedures enhanced protocol compliance [7–13]. In four Radiation Therapy Oncology Group (RTOG) studies compliance with the study protocol was enhanced by incorporating pre-treatment review of RT planning [8]. A Trans-Tasman Radiation Oncology Group (TROG) QA audit identified a reduction in unacceptable protocol violations due to three main factors, among which was the QA procedure itself [7]. More recently, strict RTQA procedures have been shown by TROG to have impacted on both trial protocol compliance as well as general clinical practice in prostate RT [9]. For several EORTC studies it has been shown that centres which previously participated in a Dummy Run (DR) were significantly more likely to be successful at subsequent DR attempts and delivery of protocol-compliant RT [10]. Additionally, the impact of RTQA on actual clinical trial outcome has been recently demonstrated in the setting of various cancer sites [11], stressing its importance and correlation with survival [12,13].

However, the various approaches as to how RTQA in clinical trials is performed, evaluated and described are diverse, making analysis and inter-trial comparisons of RTQA results challenging. This hampers cooperation between trial groups and impedes the exchange and interpretation of RTQA data. The costs of running an RTQA program have also increased with the introduction of new advanced technologies. This increases the need to make RTQA more efficient and streamline the QA workload demanded of clinical centres recruiting into international trials [14,15]. As shown by Pettersen et al [4] these RTQA efforts can potentially reduce the number of patients required for trials which could lead to further substantial savings and faster availability of results.

The need for a global forum on harmonisation of RTQA within clinical trials thus became apparent. After initial discussions in Göteborg during ESTRO 27 in 2008 the Global Clinical Trials RTQA Harmonisation Group (GHG) was formally established in 2010.

The goals of the GHG are:

1. Collate, homogenise and distribute information regarding the RTQA standards of the clinical trial groups,
2. Provide a platform for prospective discussions on new RTQA procedures, software tools, guidelines and policies of trial groups and
3. Provide a framework to endorse existing and future RTQA procedures and guidelines across various trial groups.

Each organisation will have the opportunity to endorse RTQA procedures from other organisations and thus accept them much faster in future collaborative trials.

In Table 1 the human resources and number of intergroup trials of the steering committee members of the GHG are given. Further information about terms of reference and current and future projects can be found on its website: www.RTQAHarmonisation.org.

All RTQA groups and organisations participate in international collaborative work to some degree, although there are differences between the USA and all other groups. These differences can be explained by the differences in the funding levels and that most USA RTQA groups only work with NCI funded clinical trials mainly operated in North America [16]. Recently, the North American RTQA organisations have joined forces in the new Imaging and Radiation Oncology Core (IROC) group. The dedicated human resources also vary significantly, most likely due to differences in the QA philosophy of the funding agencies and their commitment to RTQA, although most of the GHG members have at least one Radiation Oncologist, one Medical Physicist and one Radiation Technologist dedicated full time to RTQA.

Until now the GHG has contributed to the harmonisation of naming conventions [17], strategies to develop an efficient evidence-based clinical trials RTQA system [14] and the development of a global model for the international recognition of the activities of national and regional Dosimetry Audit Networks [18]. Currently, each trial group has defined its own RTQA procedures [10,19–24] that differ significantly in number, naming conventions and implementation methods [22,25–31]. The GHG is addressing this by collating all RTQA procedures of each member, comparing them and proposing common, harmonised names and procedures.

Although RTQA has been proven to be effective, international differences hamper intergroup collaboration. The Global Clinical Trials RTQA Harmonisation Group has been established to reduce those differences, capitalise on the range of expertise available internationally, increase the power of RT clinical trials, deliver consistency in the reporting of trial quality factors and facilitate the undertaking of effective multi-national trials and data analysis. Although important progress has already been made, many challenges remain to be addressed.

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Table 1

RTQA within each of the current GHG steering committee members as of August 2013.

GHG member	Year of RTQA implementation	Current human resources	Current number of intergroup trials and RTQA projects
EORTC–ROG	1982	Full time: 1 radiation oncologist, 1 medical physicist, 1 radiation technologist	9
		In kind: ROG members	
IAEA	1969	Full time: 4 radiation oncologists, 3 medical physicists, 1 lab technician, administrative support, an individual data management centre per trial	11
		In kind: 1 Medical Physicist	
ITC	1994	Full time: 2 medical physicists, 2 informaticists, 3 data managers	45
JCOG	1999	In kind: 18 radiation oncologists, 12 medical physicists	5
RTTQA	1987	Full time: 1 radiation oncologist, 3 medical physicists, 3 radiation technologists	6
		Part-time: 1 radiation oncologist, 17 medical physicists, 3 radiation technologists, 1 dosimetrist, 2 IT support, 1 administrative support	
		In kind: 3 medical physicists	
QARC	1980	Full-time:1.5 Radiation Oncologists, 0.5 Medical Physicist, 4.1 Research Dosimetrists, 4 Informatics Support Personnel, 9.5 Data Managers, 3 Administrative Support Personnel.	54
RPC	1968	Full time: 7 medical physicists, 3.5 research dosimetrists, 3 IT support, 6 administrative support employees, 5 optically-stimulated/thermoluminescent dosimeter technicians, 4 physicist assistants, 0.5 machinist	50
RTOG	1968	Full time: 2 medical physicists, 5 dosimetrists, 1 data assistant & credentialing, 1 administrative support	67
TROG	1989	Full time: 1 manager, 1 radiation therapist, 0.4 medical physicist, 1 research officer, 0.5 IT support. For software support: 1 programmer, 1 physicist	9
		In kind: TROG members	