End to end QA in image guided and adaptive radiation therapy

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Abstract. It has been suggested that modern radiation therapy could benefit from adopting the “End to End” (E2E) type of testing developed originally in computer science to determine whether applications and systems work as required under real-world scenarios. The motivation for adopting E2E techniques for image guided adaptive radiation therapy validation is to extend beyond current common testing using standard physics QA that inherently probes only select points or systems within the IGART schema. E2E methodologies extend the testing to evaluate complete IGART processes, including the complex interchanges that occur during and throughout a patient’s treatment as clinical staff interpret and respond to information acquired during the treatment course.

While limited radiotherapy E2E QA may have been adopted periodically by clinics when implementing a new treatment technique, clinical E2E QA has been confined to date mainly to tests mediated by external auditing bodies such as IROC, the Imaging and Radiation Oncology Core in the United States. This testing often includes having the clinic in question irradiate a purpose-built phantom containing dosimeters to specific criteria under protocols set by the auditing body. The auditors then determine off site whether the clinic’s treatment process was successful by comparing the dose measurements with the intended dose delivery.

The advance of three dimensional (3D) radiation dosimeters opens the possibility for in-house E2E testing. Approaches for in-house E2E testing have been proposed for over a decade, but such comprehensive internal E2E testing has not been widely adopted. In this presentation the barriers and challenges to the development of clinical in-house E2E QA will be reviewed primarily based on the experience in Kingston.

1. Introduction
“End to End testing” is a testing method originating in computer science and used to determine whether a software application performs as required in the field: the testing is performed from start to finish under real-world scenarios. End to end (E2E) tests are designed to determine whether an application or system communicates and interacts as required for proper functionality with hardware, networks, databases and other applications. It has been proposed for over a decade [1-4] that modern radiation therapy could benefit from adopting E2E methodology in the clinic, particularly as these modern techniques advance to image guided adaptive radiation therapy (IGART). Many of these proposals have suggested that the potential for clinical E2E is facilitated by the three dimensional (3D) dosimeters and other advanced dosimeters that are being discussed throughout this conference.
The motivation for the development of in-house E2E testing is that these techniques could provide additional quality assurance (QA) that addresses one inherent feature of IGART: IGART techniques incorporate multiple processes (see Figure 1), each of which demands a complex interchange during which a patient’s treatment may be modified at various points based on decisions by clinical staff who interpret information acquired during the treatment course. While physics QA would have been performed to validate the hardware used in, or systems in place at, individual steps in the process (e.g., through machine QA) such conventional QA does not by its nature validate the overall treatment process. Establishing regular in-house E2E quality assurance (QA) within treatment clinics would facilitate more regular validation of the processes involved in modern radiation therapy.

![Figure 1](image-url)

**Figure 1.** An illustration that captures the nature of the processes that can be ascribed to image guided adaptive radiation therapy. Some of the adaptive processes, particularly for intrafraction patient set up correction and motion management, are already in common clinical practice, as are some interfraction corrections, for example, plan adaptation with patient volume changes through the course of the treatment. Other processes, such as adaptive response to deformation of targets and organ at risks and dose correction to account for dose coverage mismatch in previous fractions, are still in development.

2. **Current E2E Radiotherapy Testing in the Clinic**
Currently clinical radiotherapy E2E QA is practiced only selectively in the clinic. One common utilization of E2E testing occurs when a cancer centre joins a cooperative multi-centre clinical trial [5,6]. The validation and acceptance criteria from the clinical trial group will generally include an evaluation and review of the technical components of a clinic’s radiation planning and delivery capabilities. This review will generally include an E2E test and audit mediated by an external auditing...
body such as IROC-H, the Imaging and Radiation Oncology Core-Houston, TX. The IROC-H E2E testing incorporates a component in which specific purpose-built IROC phantoms containing imaging markers and dosimeters are irradiated by the centre to specific criteria under the planning and treatment protocols set by IROC-H. The auditing centre validates that the treatment process was successful by comparing the dosimetry measurements with the intended dose delivery criteria. A detailed analysis of external audits is beyond the scope of this report, but there are excellent reviews in the literature; those by Ibbott [5] and Followill et al. [6] are particularly well detailed.

There are some general observations one can make from the experience of these external E2E audits [5,6]. The first is that in spite of the fact that the vast majority of centres coming into the external audits were well established in the IMRT and advanced IGART techniques being audited with well-defined in-house physics QA programs, a significant fraction of centres did not pass the initial IROC-H audits, particularly in the early days of the testing. The E2E testing indicated that some previously unidentified deficiencies still existed somewhere in the complete treatment chain being audited. Secondly, as time went on, the passing rates for the audits with the particular phantoms used for specific treatment sites (e.g., head and neck, lung, prostate, etc.) generally all improved consistently [6]. For example between 2001, when first introduced, and 2011, the pass rate for the IROC-H head and neck phantom improved from 61% to 91% [5]. The evidence from external audits has shown that regular IGRT process QA can help improve the consistency of IGRT delivery within a specific clinic and across institutions that participate in cooperative clinical trials.

A second implementation of clinical E2E testing that occurs more regularly in a clinic is during the development, commissioning and implementation of treatment techniques new to the cancer centre. The implementation of rigorous commissioning and proactive testing has resulted in part because of the treatment communities’ experience with the external audits described above. The results from the IROC-H type audits have identified that prior in-house testing using phantom based planning and irradiation to ensure that trial protocols are well understood and deliverable before the external audit help improve audit results. Many in the community have extended such prior testing to the commissioning of new advanced treatment techniques they are adopting in the clinic. An example of such phantom based E2E testing was reported in the very early days of 3D dosimetry [7]. Figure 2 below shows some examples of such E2E approaches in Kingston. We have over many years adopted a strategy of testing new techniques on purpose-built phantoms before a first patient is irradiated with that technique. Depending on the technique the test phantoms may be anthropomorphic, in order to best test required patient set-up procedures or to better mimic internal structures for dosimetry evaluation. In some cases (e.g., for testing fractionated stereotactic radiation therapy (FSRT) delivery), more conventional ‘physics type’ phantoms have been used because they can better accommodate well positioned dosimeters [10]. In all cases the process has been to CT image, plan and irradiate the phantom with the same procedures as would be used on a patient. Such E2E validation has proved a valuable component of technical commissioning. The testing has helped identify some technical and process challenges and has informed modifications of the planned approaches for the new technique prior to patient use.

The already adopted external and internal commissioning E2E testing described in the last three paragraphs provides a strong indication that clinical programs benefit from E2E testing. However, it has been noted [6] that these current E2E testing approaches only present a validation of the IGART protocol being tested at one specific point in time. Hence it is a snapshot that may not continue to reflect conditions in the clinic as techniques become more familiar and less special, as processes evolve, and as staff change. This suggests that more regular E2E testing, perhaps a few times a year for some of the more involved treatment protocols, may be indicated.

3. Advancing E2E Testing in the Radiotherapy Clinic

The discussion above motivates the main points of this brief review: i) that modern radiation therapy would benefit from more regular in-house E2E testing for clinical IGART process quality control, and ii) that such in-house E2E QA is feasible because the systems to enable such testing are now in place.
The availability of improved radiation dosimeters (both 3D and other) that can be inserted into phantoms, the ability of treatment planning systems dose calculation algorithms to accommodate that phantoms used are not perfectly anthropomorphic or tissue equivalent, and the increased availability of phantoms (purchased or manufactured in-house, see Figure 3) all make regular in-house E2E testing achievable. And vendors such as GeVero [Poland, www.polygevero.com], Heuris Pharma [USA, www.presage3d.com], MGS Research Inc. [USA, www.mgsresearch.com], Modus QA [Canada, www.modusqa.com], and RT Safe [Greece, www.rt-safe.com] are now providing tests tools (including dosimeters, phantoms or phantom inserts, and data analysis services) to assist in the regular adoption of E2E within the clinic.

Figure 2. Examples of E2E testing performed in Kingston during the implementation and commissioning of two advance radiation therapy techniques (see text). The top row (a-c) shows the in-house built anthropomorphic phantom and sample results of 3D IMRT delivery validation with a Fricke Gel 3D dosimeter [8]. The dose measurements (c) could be compared directly to (b) the planned dose distribution from the Varian Eclipse [Varian Medical, Palo Alto, US] doses. The bottom row shows the commissioning E2E testing for a VMAT enabled fractionated stereotactic radiation therapy (FSRT) delivery [9] using a solid phantom (d) which could hold various detectors including film (e). Panel (f) shows the correlation of the dosimetric measurements used to evaluate the integrity of the dose delivery prior to the first patients being irradiated.

There is one further observation from the E2E testing practices described in the previous section 2 above that should be noted before describing the recommended format for in-house E2E testing that will be proposed below. The E2E testing already adopted as described above is often limited in that the work from imaging, through set-up, to dose delivery is in most cases performed solely by members of the physics department. Thus the testing is, in some regards, artificial as it tests what potentially is achievable in the clinic but does not test the process with the specific personnel who will be treating the patient once the technique is implemented. (Although one might argue that some aspects of the testing, particularly the phantom set-up and on board image verification, might give better results if more experienced treatment staff are involved.) Clinical E2E testing will more appropriately and fully assess that a specific IGART treatment process is working as intended if the very staff involved in the
information analysis and treatment adaptation decisions that govern the process during a patient’s treatment are the staff involved in the various stages of phantom manipulation in the E2E testing.

![Figure 3](image1.png) ![Figure 3](image2.png) ![Figure 3](image3.png)

**Figure 3.** The evolution of head phantoms for various clinical QA and E2E testing development in Kingston. The phantoms are designed to hold various dosimetry systems in geometries relevant to the clinical process being tested. From left to right: a) the initial H&N phantom for IMRT validation [8]; b) a wax phantom to test bolus placement under masks as tumour size changes and gaps appear [11]; and c) our newest phantom 3D printed for ongoing E2E QA. All phantoms mimic a Rando phantom included in the middle panel. The grey skull in the rightmost phantom has been printed with doped material to simulate bone electron density, the surface shell has been designed to obscure the geometric configuration of the interior phantom (which is modifiable) when the phantom is manipulated for imaging or treatment by the radiation therapy staff.

The development of specific in-house E2E tests to provide regular process control for some modern image-guided adaptive radiation therapy treatment commissioning should be guided by the experience from external auditing groups and from past internal treatment commissioning. The E2E test should be designed so that the testing procedure mimics the specific IGART process as it is to be used on a patient. Some phantom with specific testing systems would be prepared in-house, or perhaps purchased from a vendor. (Note, the rest of this description will reflect our experience that the testing system incorporated in the phantom has typically been some dosimeter, either point, 2D, or 3D, depending on the test). In any case the physics staff would prepare or purchase the dosimeter from a commercial vendor (examples of in-house systems would include radiochromic leucodye micelle gel, Frick-gel or a polymer-gel; commercial systems might include radiochromic film, ClearView gels or PRESAGE radiochromic plastics). The staff would insert the dosimeter into some anthropomorphic or purpose-built phantom which would then be treated by the radiation therapy team as if the phantom were a patient. During this testing, the E2E QA would not be performed solely by the physics staff but rather by the whole clinical treatment team: planning therapists would perform CT simulation; radiation oncologists would contour structures that could be delineated in the target (perhaps using targeting modules that could be inserted in the anthropomorphic phantom); planners or dosimetrists would plan the delivery on the treatment planning system; and treatment therapists would deliver the treatment using the IGART approaches being assessed. This testing could extend to whichever adaptive processes are in regular practice in the clinic: for example, simple setup verification and repositioning under cone beam CT or under MR on an MR-linac, specific high precision treatments such as FSRT, or perhaps an adaptive procedure following tumour deformation over multiple fractions. At the end of the treatment process the physics group would remove and image the 3D dosimeter, register the dose data against the treatment planning dose distribution, and evaluate the results. If the clinical E2E QA passes some previously established scoring metrics (a topic in itself [6]) then the process being tested will have been shown to be running as intended.

Note that the E2E QA tests whether ALL the components of the treatment process are functioning as desired. For this reason the E2E testing cannot fully replace the other conventional or technical physics hardware or systems QA tests, firstly because the treatment hardware and technical systems must be maintained to the high standards required *a priori* for safe patient treatment, and secondly, a full understanding of the technical functioning of the equipment, supported by well-established QA
records of the system behaviour, will be needed in the case that the E2E testing fails. The specific E2E QA will have tested the whole process in its complete chain and the E2E testing itself cannot provide sufficient information to specify the exact point of breakdown. Complementary QA information will be required in any root cause analysis [6,12].

While presenting many advantages in the maintenance of high quality IGART, there are significant challenges in initiating the testing. E2E testing is resource intensive; the timing for dosimeter preparation and use presents challenges for incorporation into the regular clinical workflow. And modifying workflow to accommodate the E2E testing has human resource implications that may not be easily accommodated in clinical operation. But these constraints may be better understood and correctable as in-house E2E programs are developed and implemented. Past obstacles to E2E testing were removed when specific attention was directed to their resolution. For example, problems introduced by the timescale required for the readout and analysis of dosimetric data (particularly with 2D and 3D systems) for full analysis and comparison with intended dose delivery as planned in the treatment planning system were minimised in the last few years once specific attention was directed to the development of specific open-source [13,14] and commercial software tools for this function. Thus the resource challenges are not insurmountable barriers.

4. Conclusion
In closing, a unique advantage to the E2E testing presented here is the ability to mimic the specific adaptive IGART process as it would be applied to a patient; that is, through the complete chain of required data transfer, analysis and decision making (steps which are often judgment-based and not tested in conventional physics QA procedures). Regular (quarterly, bi-annually, etc.) performance of the E2E QA would ensure sustained adherence to the process protocols at the high levels adopted in the initial commissioning and implementation of the advanced IGART protocols that are advancing patient treatment in our cancer centres. This provides a strong motivation for advancing the clinical implementation of in-house E2E testing at this time. Hopefully this presentation will motivate the community attending this conference to direct some of their efforts and wisdom to establishing practical protocols for clinical end to end testing of specific IGART protocols utilized in their clinics.

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