Innovations in Radiotherapy Technology

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Conflicts of Interest

I.J. Feain and P. Keall are founders of Nano-X Pty Ltd and inventors on several granted and pending patents related to fixed-beam radiotherapy treatment systems. L. Court and P. Keall receive some research funding from Varian Medical Systems.

Key words

Brachytherapy, image-guided, innovation, low–middle income, planning, radiotherapy

Statement of Search Strategies Used and Sources of Information

Literature searches were conducted using keyword searches on Pubmed and Web of Science as well as reviewing reference lists of relevant journal articles found through that process. Contributing co-authors also provided new figures based on their own research and the research of their peers.

Abstract

Many low- and middle-income countries, together with remote and low socioeconomic populations within high-income countries, lack the resources and services to deal with cancer. The challenges in upgrading or introducing the necessary services are enormous, from screening and diagnosis to radiotherapy planning/treatment and quality assurance. There are severe shortages not only in equipment, but also in the capacity to train, recruit and retain staff as well as in their ongoing professional development via effective international peer-review and collaboration. Here we describe some examples of emerging technology innovations based on real-time software and cloud-based capabilities that have the potential to redress some of these areas. These include: (i) automatic treatment planning to reduce physics staffing shortages, (ii) real-time image-guided adaptive radiotherapy technologies, (iii) fixed-beam radiotherapy treatment units that use patient (rather than gantry) rotation to reduce infrastructure costs and staff-to-patient ratios, (iv) cloud-based infrastructure programmes to facilitate international collaboration and quality assurance and (v) high dose rate mobile cobalt brachytherapy techniques for intraoperative radiotherapy.

Introduction

There is a well-documented, urgent, global demand for technologically simpler, affordable, locally sustainable solutions for delivering safe and effective external beam radiotherapy [1], [2], [3]. Current approaches are unable to provide economical and well-supported technologies, particularly in low- and middle-income countries where cancer rates are highest, staff shortages are the most severe and resources are severely limited [1]. The outcome of this is little or no access to treatment in 55 countries and shortages in 80 others [2]. Even in the developed world, the tyranny of distance caused by geographically dispersed patient populations (for example in Canada, Australia and the UK) means that the conventional model of highly centralised radiotherapy networks has resulted in significantly reduced rates of radiotherapy utilisation and access to care as a function of the distance away from a centre that a patient lives [4], [5], [6], [7], [8], [9], [10].

The recommended minimum infrastructure requirements from International Atomic Energy Agency (IAEA) guidelines for a basic radiotherapy centre are: a teletherapy unit, a brachytherapy unit, a mould room, a simulator and some basic dosimetric quality assurance equipment [11]. For staffing, the minimum IAEA recommendations are one treatment planner per 300 patients and one radiation physicist per 400 patients receiving treatment annually [11]. It is estimated that, by 2020, low- and middle-income countries will have deficits of about 10 000 teletherapy units, 12 000 radiation oncologists, 10 000 medical physicists, and 29 000 radiation therapy technologists [2], [11]. These estimates are based on data sets in the public domain (e.g. IAEA), with staffing levels based on recommendations from the European Society for Radiotherapy & Oncology and IAEA [12]. Hence, there is a crucial need for radiation therapy staff at all levels, in addition to the need for corresponding training and ongoing professional development for these individuals. The training burden is enormous: for medical physicists, most guidelines recommend a 2–3 year internship or residency, often after completion of medical physics graduate school [13], [14], [15]. Although various educational initiatives bring young radiation oncologists and medical physicists from low- and middle-income countries to academic cancer centres in high-income countries, they are often insufficient in addressing the current and future staffing deficits [16]. Furthermore, the failure of professionals who receive training in a high-income country to return home after training in the high-income countries is a historical challenge in radiation oncology and other fields [17], [18], [19].

Developing and executing on innovative and locally sustainable radiotherapy solutions requires co-operation and co-ordination between academia, hospital, government, private enterprise and non-governmental organisations. There are many marvellous recent examples that serve to highlight the impact strong collaborations can have on redressing the staggering global underutilisation of radiotherapy (e.g. [20], [21]).

Here we describe some innovative technology developments across the radiotherapy ecosystem with the potential to provide treatments with affordable state-of-the-art technology. Utilising real-time control systems, automation and cloud-based infrastructure that is now widely available allows lean innovation in radiotherapy technology with the potential to deliver affordable solutions that are neither obsolete nor second-rate [22], [23] and enables collaboration across borders. Each of these innovations targets a different part of the radiotherapy treatment ecosystem but all aim to transform global access to safe, high-quality, accurate radiotherapy.

Automated Planning

In many countries, the roles of treatment planner and medical radiation physicist are combined. In some countries, planning responsibilities even fall to radiation oncologists [12]. For both of these scenarios, fully automated treatment planning could reduce the severe workforce shortages of medical physicists and radiation oncologists [11]. Automated planning requires a much-reduced skillset compared with manual planning, meaning that training requirements could be considerably lowered and that lesser skilled staff could manage routine planning activities.

Before 2000, much work was spent on automation of treatment-planning decisions in conventional radiotherapy, such as determining wedge filters and beam weights [24], [25] and beam orientations [26]. With the emergence of intensity-modulated radiotherapy (IMRT) [27], [28], [29], most of these efforts were redirected to the automatic delineation of normal tissues and targets [30], [31] and plan optimisation [27], [32]. However, the clinical introduction of automated treatment planning overall has been slow. The many reasons for this include the complexity of several advanced treatments (e.g. IMRT) that have become the standard of care in high-resource settings, and the requirements for these treatments (e.g. accuracy of normal tissue delineation) can be very high. A recent point/counterpoint article [33] in the journal Medical Physics debated whether, within the next 10 years, treatment planning will become fully automated without the need for human intervention. The arguments against automated treatment planning were focused on examples of treatments that remain difficult to automate, such as bilateral post-implant chest wall irradiation. There are, however, many simpler clinical situations that are possible to fully automate. Examples include four-field box treatments used to treat cervical cancer, which a group at The University of Texas MD Anderson Cancer Centre has automated as part of a project to create a radiation planning assistant for automatically planning patients for low-resource settings [34]. Their approach, illustrated via a process-oriented workflow in Figure 1, uses standardised treatment approaches to automatically create radiation plans for cervix, breast and head/neck treatments, including automatic secondary checks of many of the planning tasks, including contouring [35].

Although automated treatment planning has yet to be fully realised in a clinical setting, it will probably occur within 5 years. Much of the necessary research and development has already taken place, leaving the essential steps of integration (into a commercial planning system), deployment and training. Such an achievement could realise significant reductions in the number of physicists needed for planning purposes.

Real-time Adaptive Image-guided Radiotherapy

The inclusion of image guidance and adaptation enables a change in the patient set-up paradigm, from the current iterative external/internal alignment to a patient adaptive approach. Currently, patients are typically set-up for treatment using one or a combination of room lasers, indexing systems and X-ray imaging. The patient position is measured, corrected and often measured again before treatment. In the patient adaptive approach, variations in the patient position, inter- and intrafraction changes can be dosimetrically accounted for, even for large displacements. For example, for conformal prostate radiotherapy, patient positioning shifts of up to 10 cm could be robustly adapted to via geometry-based adaptation [36] and intrafraction organ motion of 2 cm could be similarly accounted for [37]. For IMRT it has been shown that, with geometry-based adaptation, plan quality was maintained despite target rotations of up to five degrees and translations up to 15 mm [38]. Having the system adapt to the patient, rather than adapting the patient to the system, will improve workflow when automation is sufficiently fast.

Marker-based real-time image guidance has been a clinical reality in real-time radiotherapy and CyberKnife [39] systems for over a decade and has recently been implemented on a single-kV imager gantry rotating system [40]. For widespread use, real-time image-guided radiotherapy will probably need markerless solutions. A variety of kV-based and MV-based solutions have been proposed [39], [41], [42], [43]. Much work is going into the broader clinical translation for these promising markerless methods. Once the real-time image-guided radiotherapy system determines the tumour location, the task of real-time adaptation to this motion can be achieved via multileaf collimator (MLC) tracking or couch tracking. MLC tracking technology has been clinically implemented for translational target tracking [44] and has been shown in phantom cases to account for tumour rotation [45] and deformation [46]. Couch tracking has been investigated in several studies, but has yet to be clinically implemented [47], [48], [49]. A recently published comparison of four tracking technologies (CyberKnife, Vero, MLC and couch tracking) showed that all systems are capable of highly accurate target delivery in the presence of motion, and that large treatment errors resulted when motion was not explicitly accounted for [50].

Real-time image guidance has been implemented on widely available systems. Both MLC and couch tracking capabilities are software adaptations to these widely available solutions.

Fixed-beam Radiotherapy Treatment Units using Real-time Adaptive Image-guided Radiotherapy

Simplified gantry designs are emerging for magnetic resonance imaging–linac therapy, proton and ion therapy, and medical applications of synchrotron radiation [51], [52], [53]. In all cases, the engineering complexities associated with rotating the treatment gantries (rather than the patients) are either impractical or very costly [54]. Patient rotation is in clinical use at a few specialised centres [55], [56], [57] with a number of other seated rotation solutions now emerging on the market. Both vertical and horizontal patient rotation solutions are also under development for MV photon radiotherapy applications [59], [60], [61]. The size, surface area footprint and shielding requirements for the horizontal patient rotation solution have been estimated to be three times smaller than a typical linac available on the global market today [59]. Real-time, adaptive, image-guided therapies (described above) allow for curative treatments including stereotactic body radiation therapy (SBRT) and volumetric modulated arc therapy, while relaxing some of the patient alignment (and hence staff-to-patient ratio) requirements. Delivering hypofractionated image-guided radiotherapy treatments allows for increased patient throughput. Fixed-beam linacs could deliver superior treatments at the same cost level as existing low-cost radiotherapy units available in some low- and middle-income countries.

The Nano-X Tatum Horizontal Patient Rotation Solution

Nano-X Tatum is one solution under development for a fixed-beam linac using horizontal patient rotation [52], [54], [59] and on-board imaging capabilities to enable real-time image-guided motion management. The hardware for this system will comprise five main components, the minimum requirements for each being: (i) 6 MV linear accelerator, (ii) MLC tracking capability, (iii) MV electronic portal imaging device detector, (iv) kV imaging source and detector, (v) patient rotation pod and (vi) real-time control of all of the above.

The Nano-X Tatum patient rotation pod is shown in Figure 2. The principal criteria for the pod design were safety, real-time control, short treatment times and patient comfort and tolerance. Patient and user safety are ensured through triple redundancies in communication, interlocks, emergency stops and manual override protocols. Short treatment times are enabled through fast (1 min) patient ingress and egress. Immobilising primary straps and secondary pneumatic air bags facilitate patient comfort and tolerance. Once commissioning of the pod is complete, it will be integrated with a refurbished linac for end-to-end pre-clinical demonstration.

Gravitational Motion and Deformation

Patient rotation challenges conventional image guidance and immobilisation techniques, while reducing the size, cost and service burden of a rotating gantry. The gravitational effects on anatomy caused by immobilised horizontal rotation are now being investigated with pre-clinical and preliminary work suggesting deformation is at most two to three times larger than the relatively small deformation caused by respiratory motion. Real-time image guidance and adaptation will be used to maintain treatment quality, which in a general sense means that a larger fraction of patients can be offered shorter-course hypofractionated treatments. Patient motion will be minimised with semi-automated set-up and immobilisation. Nano-X machines will adapt in real-time for all residual motion and deformation.

Nano-X Treatment Workflow

Patients are scanned on a conventional computed tomography planning system and their treatment plan is calculated. Patients are transferred into the Nano-X pod and immobilised. A pre-treatment cone-beam computed tomography is acquired by rotating the patient once. These steps all align with the conventional protocol for modern radiotherapy with on-board imaging capabilities. Volumetric images of the patient anatomy at each treatment angle are reconstructed (for IMRT and conformal treatments; volumetric modulated arc therapy treatments are dealt with slightly differently). The planning computed tomography volume is warped with correct correspondence to the volumetric cone-beam computed tomography and the treatment plan is adapted accordingly. Patients are treated with the adapted plan and residual tumour motion can then be monitored and adapted with real-time adaptive techniques similar to those described above.

Cloud-based Collaboration for Radiotherapy Clinical Trials, Research and Training

Interobserver variability in target delineation is by far the single largest systematic uncertainty in the delivery of accurate radiotherapy [64], [65]. Proactive collaboration and expert peer review across international borders, together with strict credentialing and data quality assurance requirements, could go a long way in facilitating international harmonisation and better patient outcomes through training, credentialing and international clinical trials with faster accrual of patient cohorts [66].

A remotely accessible cloud-based electronic platform (CEP) has been developed to facilitate collaboration among radiation oncologists around the world [67]. The platform is secure and efficient and appeals to experts from diverse populations and demographics. A patient's data created at one institution are immediately available for review at another institution using only a web browser. Immediate feedback between the institutions occurs, facilitating uniformity across clinics irrespective of geographical location. This not only ensures trial protocol compliance and high standards of uniformity, but also facilitates training and credentialing regardless of geographical location.

The Cloud-based Electronic Platform

The CEP specifically confronts the issue of peer review of advanced radiotherapy planning and delivery techniques in the pursuit of international collaboration across borders regardless of socioeconomic status. Cloud-based collaboration has the potential to significantly improve quality, safety and accessibility of advanced radiotherapy techniques and enhance capabilities of institutions in global health research and training. It provides an environment in which radiation oncologists worldwide can receive, share and analyse multimodality data to facilitate expert review, second opinion and international clinical trials in radiotherapy.

The CEP requires minimum local operational resources. It stores all data in a cloud while making it possible to cache data locally for full-offline operations, obviating the need for local backup of data. The CEP meets the following design criteria:

(i) Users securely upload and download imaging from modalities including computerised tomography, magnetic resonance imaging, secondary capture, digital radiography, portal images and digitally reconstructed radiography as well as radiotherapy data objects (DICOM, scanned images, treatment plans, etc.).

(ii) Data are automatically registered and entered into a database and are never overwritten.

(iii) Patient confidentiality is maintained throughout the process. A hierarchical privilege-based remote access is available for users of the system.

(iv) Submitted clinical data are processed automatically and made immediately available to download worldwide using a web browser and custom-built application.

(v) Data objects are annotatable on a graphic user interface with the support of data authoring and versioning control.

Figure 3a shows the process-oriented view of the CEP events from the users' perspective. Clinical data flow from treatment planning systems and/or imaging devices to a local PC that runs the data processing application (DPA) software. DPA software anonymises and encrypts radiotherapy data and uploads it to the cloud server via web services. An electronic notification is immediately sent in the form of an email with a URL to the reviewer/s from a stored list in the DPA software. This URL takes them directly to the web portal containing information on all accessible data for that patient. The submitted data become immediately logged into an electronic folder, which can be viewed by the reviewer either via a web browser in the cloud for rapid review or by downloading it from the cloud to a local PC for an in-depth review. Both options are provided to cope with varied and variable network bandwidths. The Microsoft Silverlight 'thin client' interface allows instant web-based access to DICOM images, secondary capture images and pertinent treatment planning information. The data review tools are adequate for the review of delineated anatomy and include zoom, pan, measure, window and level, annotate, turn 'on/off' segmented structure overlays and drawing tools. Figure 3b shows an example of a web page emulating the desired functionalities of a peer review tool.

High Dose Rate Co-60 Brachytherapy for Intraoperative Radiotherapy

Co-60 has recently been incorporated for use in high dose rate (HDR) brachytherapy [68], [69] and is commercially available integrated in an afterloader [70]. Co-60 HDR brachytherapy afterloaders offer clinically established treatments for many type of cancers (head and neck cancers, endobronchial and oesophageal cancers, gynaecological cancers, breast cancers and prostate cancer). Because Co-60 HDR brachytherapy afterloader machines only require a source exchange every 5 years, they significantly reduce the operating and logistical overheads associated with other available HDR afterloaders using, for example, Ir-192, which require a source exchange every 3 months [20].

Another innovation of Co-60 HDR is in the integration of afterloader machines with mobile units for mobile intraoperative radiotherapy (IORT). IORT is well established and can be delivered using these systems in a variety of malignancies, especially when primary tumour control has a critical implication for patient morbidity and quality of life [71], [72]. HDR IORT treatments are delivered after resection of the tumour. A single large radiation dose is delivered to the tumour bed or margin at risk for local failure while excluding or limiting the dose to adjacent sensitive organs and structures. HDR IORT treatments could be a useful replacement option for when access to external beam radiotherapy is limited (Figure 4).

The use of Co-60 HDR afterloader machines would require special attention to shielding requirement and logistics. They can only be operated in shielded Co-60 rooms or shielded operating rooms where the number of HDR procedures performed per week should be taken into consideration.

Conclusion

Here we have described several examples of innovative technology developments across the radiotherapy ecosystem. These examples are all linked by a shared hypothesis that by moving the complexities of technology from hardware and staffing to automation and software, it becomes possible to re-imagine global access to safe, high-quality, accurate and locally sustainable radiotherapy with software approaches, real-time algorithms and cloud-based capabilities. The examples described in this paper are by no means exhaustive, representing only a small selection of many innovations at various stages of clinical realisation that can be directed to improve cancer care in underserved regions. The ability to execute on innovative technology developments unquestionably requires collaboration and coordination between academia, hospital, government, private enterprise and non-governmental organisations with a shared vision and short-term, mid-term and long-term strategies.

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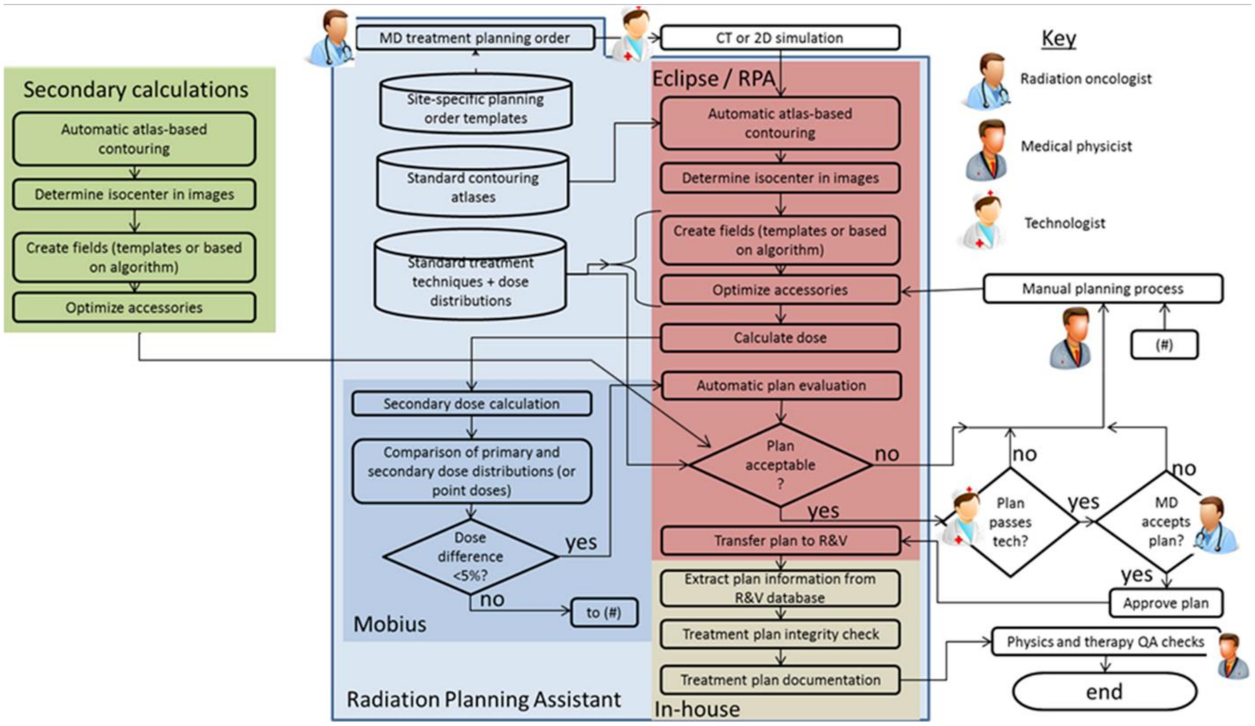

Fig 1. Workflow for an automated treatment planning system (radiotherapy planning assistant) being developed at The University of Texas MD Anderson Cancer Center. The people icons indicate where user interaction is needed. All other steps are automated.

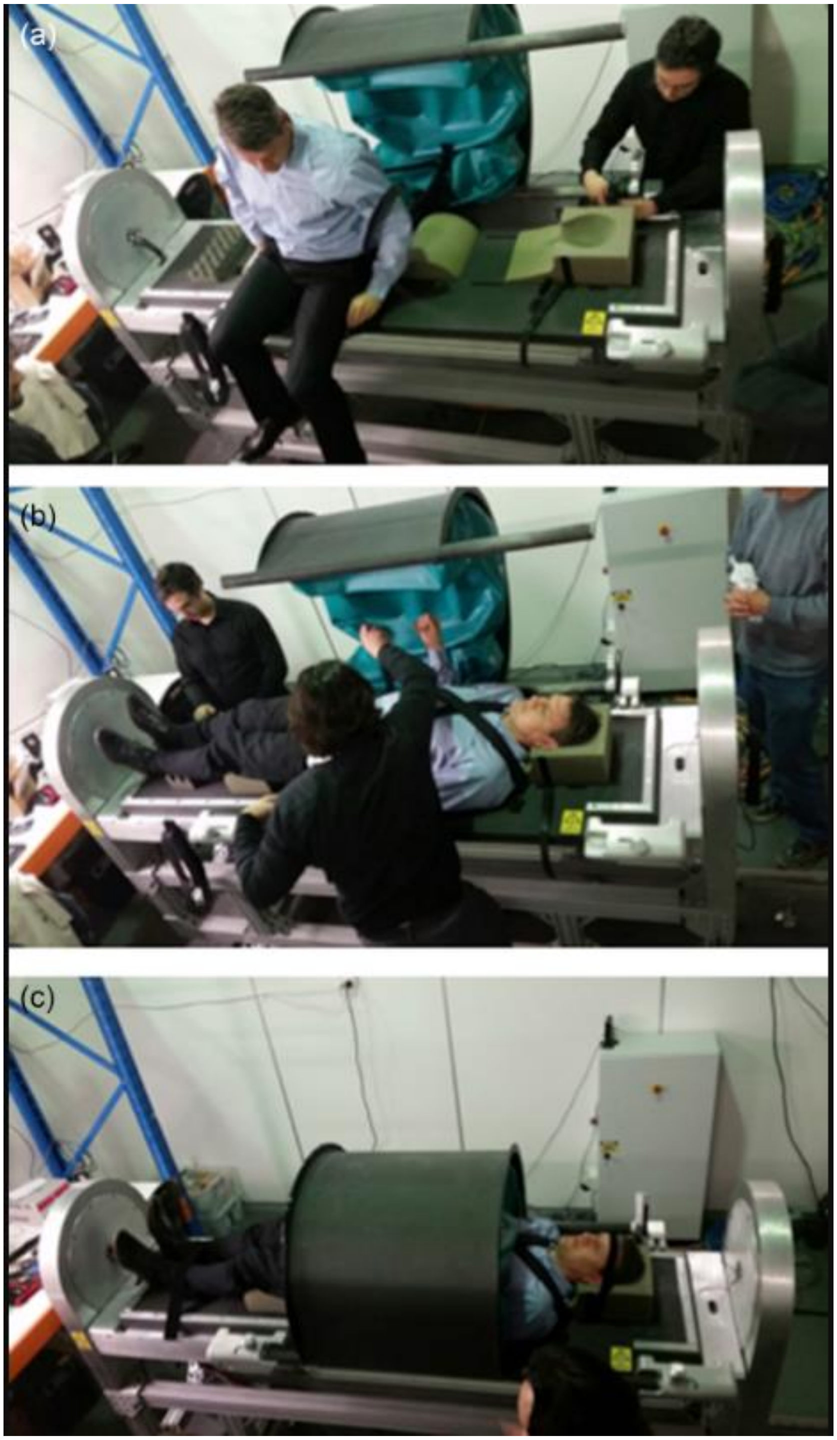

Fig 2. Nano-X Tatum rotation pod stages from ingress to imaging-ready position: (a) ingress at a comfortable sitting height, (b) lies down in supine position and primary restraints secured, (c) pneumatic airbag systems provide secondary immobilisation and patient comfort and security.

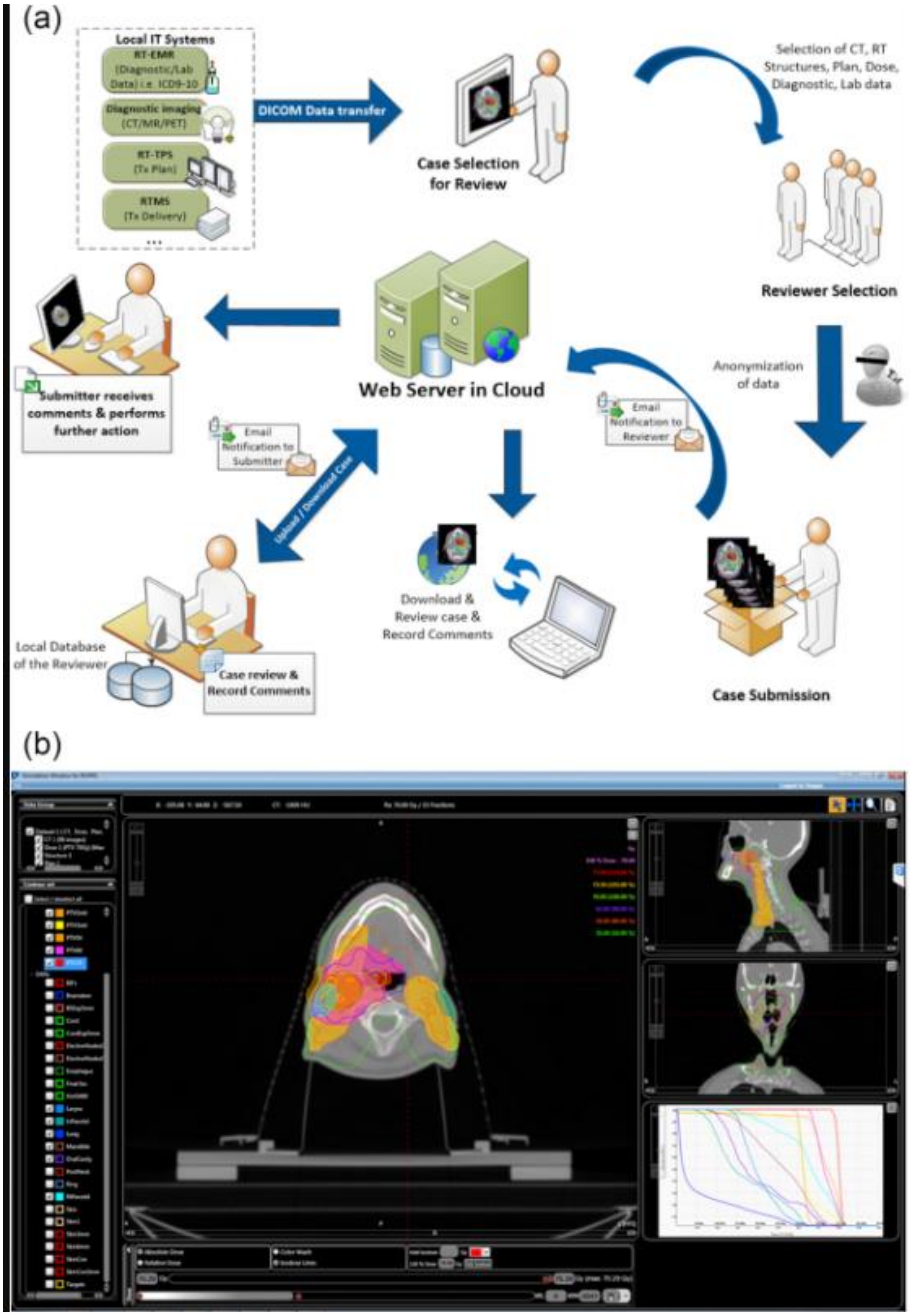

Fig 3. (a) Process-oriented view of the set of events of the cloud-based electronic platform (CEP). (b) A web page that emulates some of the desired functionalities of the CEP.

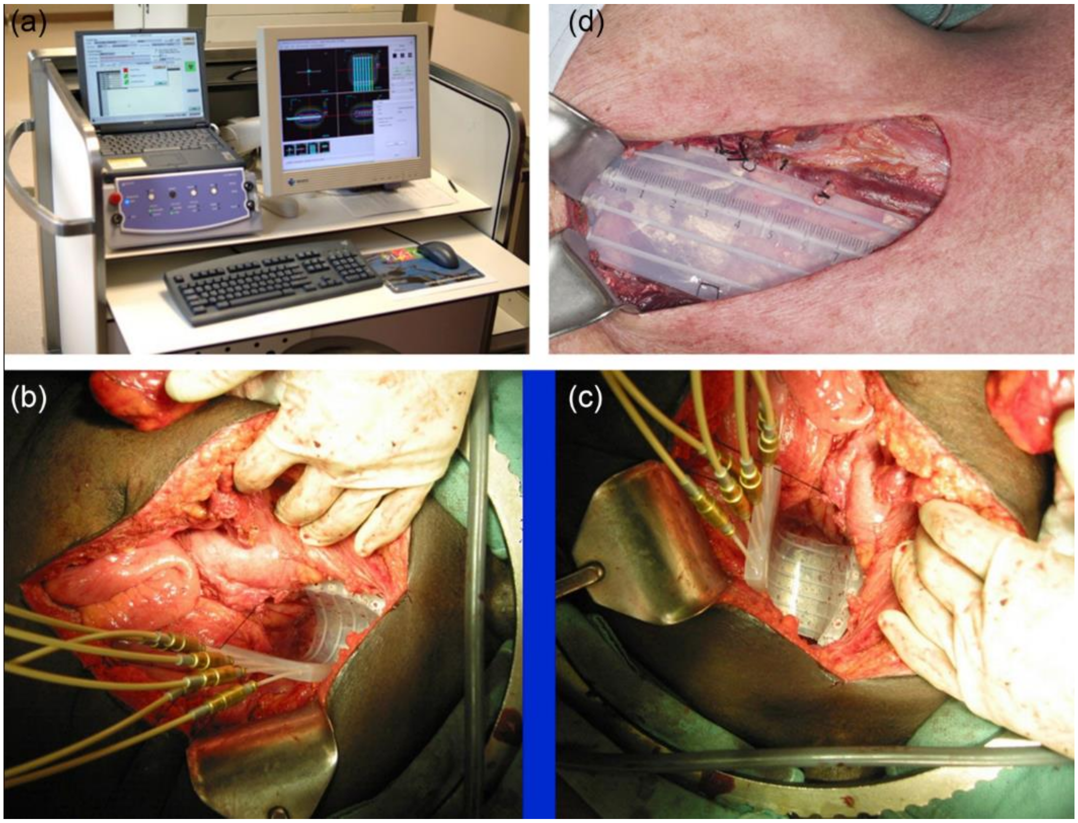

Fig 4. A mobile high dose rate brachytherapy treatment system could be used for intraoperative radiotherapy: (a) brachytherapy treatment planning system on a mobile platform, (b) an example of a HAM applicator inserted in the abdominal cavity for a colorectal cancer case, (c) another example of a HAM applicator stitched inside the neck for a head and neck cancer.