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Original contributions

An intelligent oncology workstation for the 21st century

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The 21st century will see the routine clinical use of improved radiotherapy treatment techniques, such as intensity modulated radiation therapy (IMRT). An essential feature for the implementation of IMRT is the ability to identify precisely the location of body structures, particularly those involved with cancer and surrounding uninvolved regions, which should receive minimal dose. The aim of this paper is to introduce the concept of an intelligent oncology workstation: a one-stop workstation combining the automatic delineation of structures of interest with the optimization and scheduling of radiotherapy treatment delivery.

Material and methods. Software tools have been programmed using the Matlab programming environment and C/C++. Rule based algorithms refine contours obtained using low-level image processing tools. Treatment planning optimization algorithms combine a least square methodology with multiple objective genetic algorithms.

Results. The imaging software can outline successfully regions of interest such as the bladder, rectum and pelvic bones. Optimization provides a set of solutions for coplanar beam orientation and modulation in intensity, taking into account dose delivery constraints.

Conclusions. Using clinical experience as well as the raw image data, a physician employing the workstation can improve IMRT planning with automatic identification of body organs and structures. Multiple objective genetic algorithms (MOGA) exploiting the concept of Pareto optimality offer advantages over the traditional weighted sum approach. MOGA provides clinicians with a set of equally good IMRT plans that take into account practical limitations of the treatment delivery mechanisms.

„Inteligentne" stanowisko leczenia onkologicznego na miarę XXI wieku

Należy sądzić, że w XXI wieku zostaną wprowadzone do rutynowego użycia ulepszone metody prowadzenia radioterapii, na przykład radioterapia z zastosowaniem modulowanego natężenia (IMRT - intensity modulated radiation therapy). Podstawowym warunkiem stosowania IMRT jest możliwość precyzyjnego określenia położenia poszczególnych narządów i struktur, a w szczególności określenie obszarów zajętych przez nowotwór oraz otaczających je tkanek. Umożliwia to skierowanie możliwie najniższych dawek na zdrowe tkanki. Celem niniejszej pracy jest przedstawienie „inteligentnego" stanowiska do leczenia onkologicznego - aparatu umożliwiającego automatyczne określenie, istotnych w danym przypadku, struktur oraz planującego i optymizującego podaż dawek leczących.

Materiał i metody. Zastosowano oprogramowanie Matlab i C/C++. Umożliwia ono opracowanie odpowiednich algorytmów, precyzując kontury z zastosowaniem technik obrazowania.

Wyniki. Zastosowane wyposażenie i obrazowanie umożliwia bardzo dokładne określenie struktur takich jak pęcherz moczowy, odbytnica i kości miednicy. Optymizacja zapewnia gotowe rozwiązania, umożliwiające stosowanie wiązek we wspólnych płaszczyznach oraz modulowanie natężenia dawek z uwzględnieniem koniecznych ograniczeń.

Wnioski. Lekarz obsługujący opisane „inteligentne" stanowisko jest w stanie, w oparciu o doświadczenie kliniczne i dane obrazowe, poprawić planowanie leczenia z zastosowaniem IMRT, wykorzystując automatyczną identyfikację struktur i narządów organizmu. Wielocelowane algorytmy genetyczne (MOGA), odnoszące się do idei optymalizacji wg Pareto, zapewniają przewagę nad tradycyjnie stosowaną metodą zsumowania masy. MOGA zapewnia klinicystom dobre planowanie IMRT, które uwzględnia tak wszelkie ograniczenia kliniczne, jak i mechanizmy podawania dawek.

Key words: IMRT, radiotherapy, optimization, image processing, constraints, multiple objectives
Słowa kluczowe: IMRT, radioterapia, optymizacja, techniki obrazowania, ograniczenia, wielocelowość

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Introduction

The diagnosis and treatment of cancer in the early 1900s was first revolutionised by the seminal discoveries of X-rays (1895), radioactivity (1896) and radium (1898). Then by the 1980s significant technological advances had occurred in the development and application of imaging devices (e.g. CT, MR and ultrasound) and of treatment planning software and treatment delivery, [1]. Not least of these in the field of radiotherapy, now usually termed radiation oncology, was the ability to plan in 3D, to optimise, and to produce truly conformal plans for individual patients [2].

The oncology workstation is being designed for external beam radiotherapy and Figure 1 illustrates central axis percentage depth dose variation for a range of photon energies, as well as for electrons and for protons. The radiotherapy machines, which deliver megavoltage beams, are highly sophisticated and modern linear accelerators are computer controlled and equipped with multileaf collimators. This presents the clinician with an armamentarium with a very wide spectrum for the treatment of cancer once the planning treatment volume (PTV) has been defined.

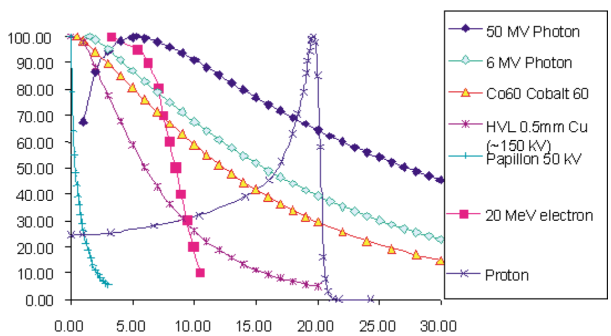


Figure 1. Comparison of central axis percentage depth doses for photons, electrons and protons

Relatively recent developments, still only available to few cancer centres, include the use of protons or heavy ions (as an alternative to photon or electron beams), which are used in order to improve the irradiation of deep-seated tumours whilst also sparing the dose to normal tissues [3-6]. This can be visualised from the proton curve in Figure 1. However, a major obstacle to the widespread use of proton beams is that their production requires the use of a cyclotron, which is often prohibitively expensive for a cancer centre, even though a cyclotron could be used to serve several treatment rooms.

For many years, before the digital computer era, treatment planning computations were performed manually and consisted mainly of only a single 2D isodose distribution plan drawn in a cross-section through the major axes of the coplanar beams, the number of which varied but was usually not greater than four for mega-voltage photon plans. The tissues, including those of the tumour, were all assumed to be of unit density material and often no account was made of air spaces due to obliquely angled radiation beams.

Current computer software provide clinicians with the means to plan treatments involving non-coplanar beams. Some of these software also include optimisation tools to help clinicians select the most appropriate beam orientation and/or beam modulation. The optimisation of the beam orientation is a complex and time consuming process. It has been shown that the optimisation of coplanar beam orientation for IMRT is mainly beneficial for a small number of beams, typically less than five [7, 8]. Above five coplanar beams, equi-spaced beams are employed for IMRT as they are close to being optimal and are more practical to implement. It has also been shown that the optimal orientation is dependent on the type of treatment used. For standard radiotherapy treatment techniques, beam entry points close to organs at risk were penalised, whilst they are favoured for IMRT due to the ability of the beam to be modulated in intensity [4, 5, 7, 8].

The selection of the type and the tuning of beam modulation devices is another important aspect of modern radiotherapy treatment planning. Beam modulation devices can be divided into two categories: *static* such as wedges or compensators and *dynamic* such as multileaf colimators (MLCs) or a MiMic device [9] with dynamically controlled leaf positioning, see Figure 2.

Wedged fields are not new, having been developed in the 1960s. However, their implementation has changed from being an individual wedge, with a fixed wedge angle, constructed of a material such as copper, to being a motorised wedge such as incorporated into the design of radiotherapy linear accelerators. The motorised wedge enables fields with any wedge angle to be applied. Wedges are currently the most commonly used beam modulation devices but their disadvantage is their inability to produce highly modulated beam profiles.

Compensators used for IMRT are usually fixed onto a *tray* at a distance from the patient. This has the advantage of preserving the skin sparing effect, whilst being able to produce highly modulated beams. This is due to the use of a highly attenuating material for the compensator design. The main drawback of compensators is the time required for their manufacture and this limits their use to a small number of fields.

MLCs produce intensity modulated beams by means of moving mechanical parts, high density tungsten leaves, following a predefined pattern during the treatment. MLCs require the use of an interpreter to transform an intensity profile into a set of leaf movements.

Modern developments in conformal radiotherapy and in IMRT [2, 3-5] are spreading from specialised research institutions to typical non-university radiotherapy clinics and as IMRT progresses, evidence is beginning to confirm the benefits of more accurate treatment [10, 11].

The major technological advances in radiotherapy equipment and in software and dosimetry development has changed the procedure of the treatment planning

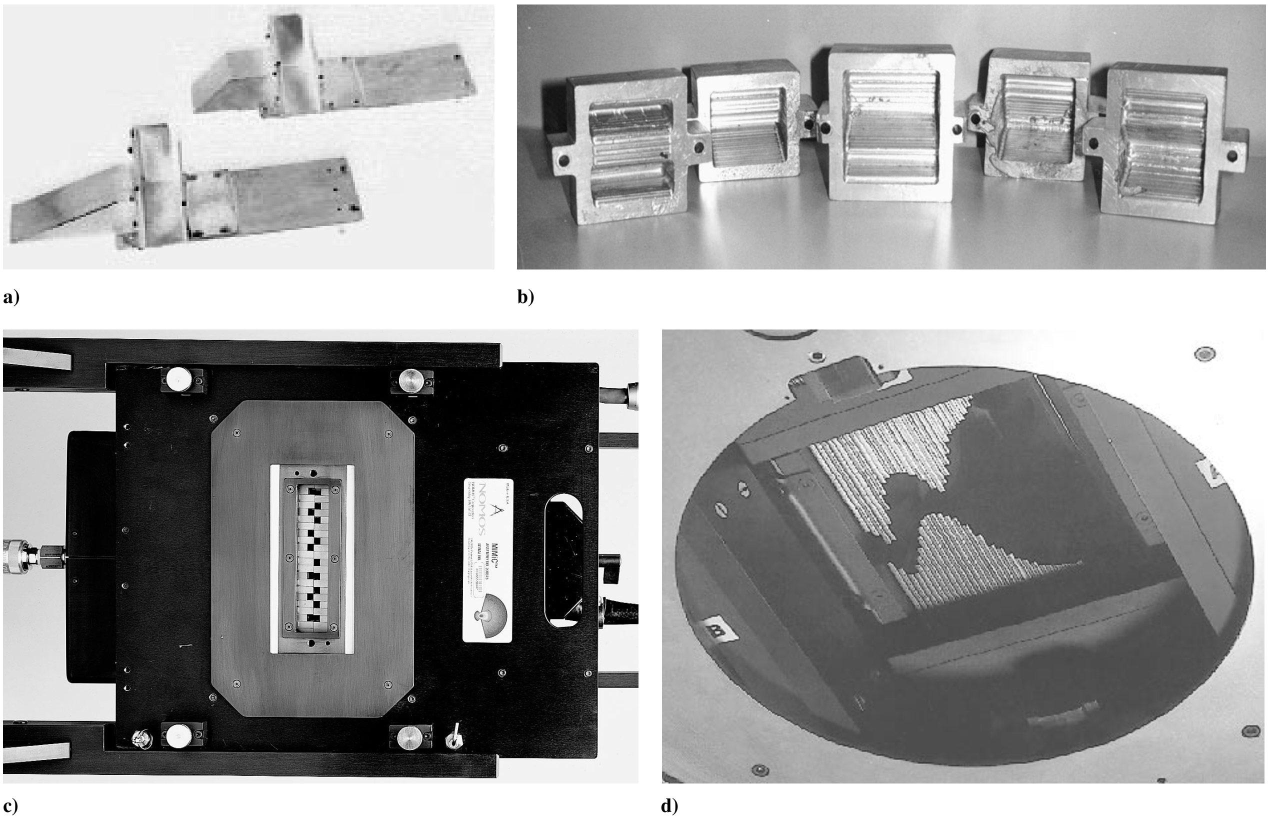


Figure 2. Beam modulation devices. [a] Wedge compensators. [b] Compensator designed for an individual patient. [c] MiMic compensator: courtesy Nomos Corporation, USA. [d] Multileaf collimator: courtesy Elekta Oncology Systems, UK

process out of all recognition from the period of 2D unit density tissue isodose distributions. This brief Introduction concludes with a flow chart for modern radiotherapy 3D planning from image acquisition to treatment verification, Figure 3. The aim of the intelligent oncology workstation is to provide the radiation oncologist with a more effective tool to conduct the planning process as outlined in Figure 3.

Material and methods

This section describes the methods employed within the intelligent oncology workstation to outline body structures and optimise the practical planning of IMRT in terms of beam orientation and beam modulation. A description of the material used for the software implementation, the *practical* demonstration of IMRT and of the influence of delivery constraints on compensators and multileaf collimators, is given.

Towards automatic image segmentation

The first stage in the planning process is to identify the regions of interest (ROIs) with respect to the treatment and the PTV to allow the selection of appropriate beam arrangements. This stage takes into consideration the effect of all possible geometrical variations and inaccuracies: such as patient movement and positioning. This is in order to ensure that the prescribed dose is actually delivered. Other ROIs to be outlined always include critical body structures and tissues that are adjacent to the PTV.

The imaging software developed facilitates the delineation of anatomical structures and tissues, including both those within the PTV and those, which are not involved by tumour spread.

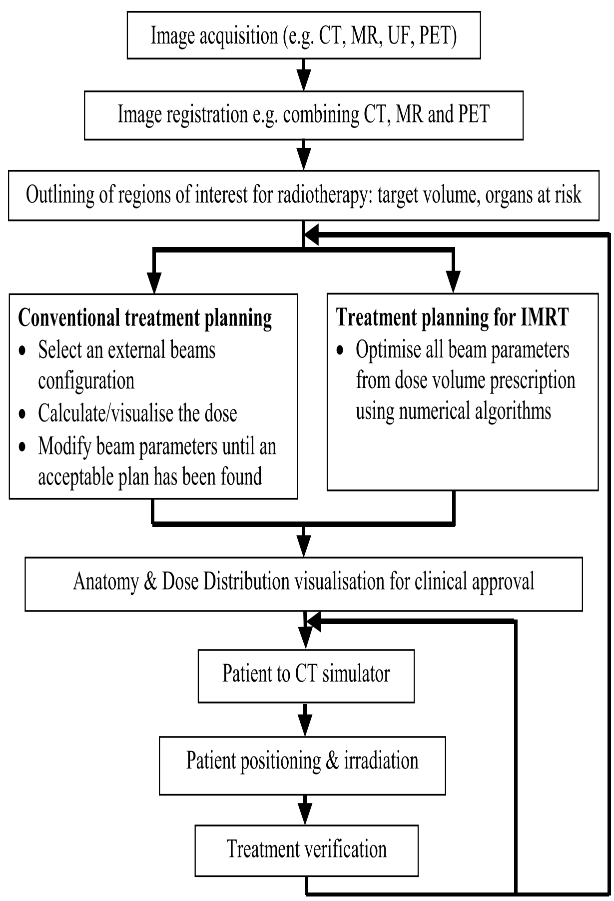


Figure 3. Flow chart of the radiotherapy treatment planning process from image acquisition to treatment verification

The outlining process is performed on computed tomography (CT) images obtained from a CT scanner. The software is based on a hybrid image segmentation technique developed 1995-98 [12, 13] Table I, and a feedback-rule based mechanism developed 1999-2002 [14, 15] Table II.

Table I. Features of the hybrid image segmentation technique [12, 13]

- Pre-processing (i.e. smoothing) to remove noise from the image that may cause subsequent algorithm to oversegment the ROIs.
- Adaptive thresholding to minimise the number of ROIs and give a first estimate of their contours.
- Two different segmentation algorithms to complete the delineation of the ROIs in a CT image.
- A merging algorithm based on a region adjacency graph to merge small ROIs and enclosed ROIs that belong to the same body structure.

Table II. Features of the feedback rule-base technique [14, 15]

- *Training.* Knowledge of anatomical regions to be delineated is gained by outlining ROIs within CT images and deriving statistical distributions for the location of their centre, periphery, shape and grey levels.
- *Ray tracing.* Making use of the expected location of the centre of the ROIs, a ray tracing technique is used to segment the organs. This exploits signal processing and filtering techniques to detect a candidate edge for the organ.
- *Voting mechanism.* Combining the edges previously found, a voting mechanism based on the expected location and grey level of the boundary pixels is used to select the most likely candidate pixel.
- *Contour smoothing.* Having obtained a set of candidate outlines, these are modified using a rule-based mechanism that rejects pixels which are different from the neighbouring pixels in terms of geographical location and grey levels.

For the hybrid segmentation technique the software was written in C/C++ with the graphical user interface implemented using MOTIF. It was subsequently ported to Linux and is able to run both on the workstation and on a PC.

The feedback rule-base software was developed using both the Matlab environment and C/C++. This can also run on workstation or on a PC. The C/C++ components of the system can also run on a network of Linux platform to investigate the potential benefits of parallel processing [15]. This feedback mechanism [14, 15] exploits *a priori* knowledge of the location and shape of organs to help the segmentation process [14].

Optimizing radiotherapy treatment

Having outlined the ROIs a treatment plan is obtained that complies with the dose regimen prescribed by the radiation oncologist. Currently it is possible to optimize coplanar beam orientation and intensity modulation in terms of wedge angle and compensator profile. The algorithms employed include deterministic techniques derived from the least squares method as well as heuristic techniques such as multiple objective genetic algorithms (MOGAs). All methods attempt to optimise several objectives that are contradictory in nature. For example, one objective may be to deliver a high uniform dose within the PTV and a second objective to deliver a low dose in various radiation sensitive body structures, which are not involved with tumour.

Traditionally a weighted sum approach combines the various objectives into a single *trade-off cost function* that can then be optimised [3, 5]. Such an approach has been refined by allowing the *weights,* which are relative importance factors associated with each objective, to be modified during an iterative search procedure [8, 20]. This type of approach allows a reduction of the weights on the objectives that can be fulfilled whilst also permitting greater emphasis to the objectives that are difficult to achieve.

The advantage of the weighted sum approach when combined with an analytical technique such as least squares is that it converges rapidly to a solution. The disadvantage is that if the initial choice of weights is not appropriate then the search has to be re-started with a new set of weights [4]. This can become a lengthy process in a clinical environment where physicians with no specialist knowledge of optimisation select the weights.

Multiple objective search techniques based on Pareto optimality [17] do not combine the objectives, but instead, attempt to determine a set of solutions that define the *trade-off* between the various objectives [4, 8]. Using such an approach, it is possible to provide the radiation oncologist with a range of solutions that focuses on delivering a high dose to tumour tissue and also delivering an extremely low dose to healthy tissues. A MOGA was employed to implement the principle of Pareto optimality [4] Table III.

Table III. Actions performed by the MOGA.

- Generate a set of candidate solutions.
- Calculate the cost associated with each objective considered in the search process.
- Calculate the distance from the Pareto optimal set using Pareto ranking.
- Modify the Pareto ranking using clinical experience of the most favourable *trade-off.*
- **+**Select a subset of solutions (i.e. a sub-population) which includes the best solution found to date, and which is to be modified with genetic algorithm operators.
- Combine and modify solutions from the previously identified sub-population.
- Calculate the cost associated with each objective considered in the search process.
- Calculate the distance from the Pareto optimal set by using Pareto ranking.
- Modify the Pareto ranking using clinical experience of the most favourable *trade-off*.
- Retain all the solutions belonging to the Pareto optimal set.
- Return to **+** for a further selection process unless a set of solutions satisfying the search criteria has been determined or a maximum number of iterations has been reached.
- Use a decision theory method to exploit additional practical information in order to determine the *best* treatment for an individual patient.

The least squares method was primarily employed to optimise the beam intensity modulation for IMRT. With the additions of constraints on the shape of the beam profile produced, the MOGA was also able to optimise plans for traditional (i.e. non-IMRT) radiotherapy delivered using wedges. It was then used to propose two or three *good* alternative sets of wedge angles and to optimise the coplanar beam orientation. In addition, the MOGA was combined with the least squares method to optimise IMRT plans.

A genetic algorithm is a guided random search technique inspired by human-like behaviour and using terminology associated with evolving natural processes such as genetics. It can be visualised as using insight, creativity, learning and exploitation to achieve solution that can potentially be globally optimal. Indeed, as opposed to deterministic search techniques such as least squares, genetic algorithms can escape local optima: although there is no guarantee that the global optima will be found. The latter may however take a huge amount of computation. Therefore the MOGA was developed in order to search for *good possible* solutions as opposed to optimal solutions.

Identifying and compensating for treatment delivery constraints

Constraints, which arise due to the dose delivery mechanism, were studied experimentally using a specially designed phantom. Once identified, some of these constraints have been incorporated within a Matlab software environment. A modified least squares method was then devised to overcome these constraints, such as those associated with the compensator manufacturing process and with the use of multileaf collimators (MLCs). It was therefore possible to ensure that the valleys to be manufactured in the compensator are sufficiently wide and force the compensators to be more regular than otherwise would have been the situation [20].

An iterative least squares optimisation procedure was performed to minimise the limitations arising from the patient support system design for IMRT. This takes into account the fact that IMRT treatments may employ a large number of beams with unusual beam orientation and several different beam orientations may be used during a treatment session. To keep the time required for a given treatment within acceptable limits, it is necessary to ensure that neither the patient or treatment couch have to be moved during treatment.

When dense support structures for the patient intersect the beam paths, unacceptable dose attenuation occurs and this attenuation is in general not taken into account at the planning stage. It is therefore necessary to ensure that the optimised beam paths do not intersect with the main couch structures, Table IV [20].

Table IV. Features of the beam-couch collision avoidance algorithm

– The geometrical characteristics of the beam path and patient support system are used to detect any intersection(s) with any parts of the treatment couch structure.
– If intersection(s) occur.
  + ■ Re-optimise the beam position using geometrical criteria such that it deviates only by a small amount from its original position.
  + Re-optimise the beam modulation for the positions previously found.
  + Return to ■ until a satisfactory plan can be found.

Experimental compensators

IMRT was originally assessed using patient specific compensators manufactured using a computer numerically controlled milling machine at the University Hospitals Coventry and Warwickshire NHS Trust. It was found that a ball nose cutter with a diameter of 6 mm offered the best compromise between speed of manufacture, tool wear and resolution of the delivered intensity modulated beam (IMB) profiles [18-20]. The compensators were made of high-density (ρ=7.27 g.cm-3, linear absorption coefficient μ=0.3 cm-1), low melting point alloy, MCP200.

Pelvic phantom for film dosimetry

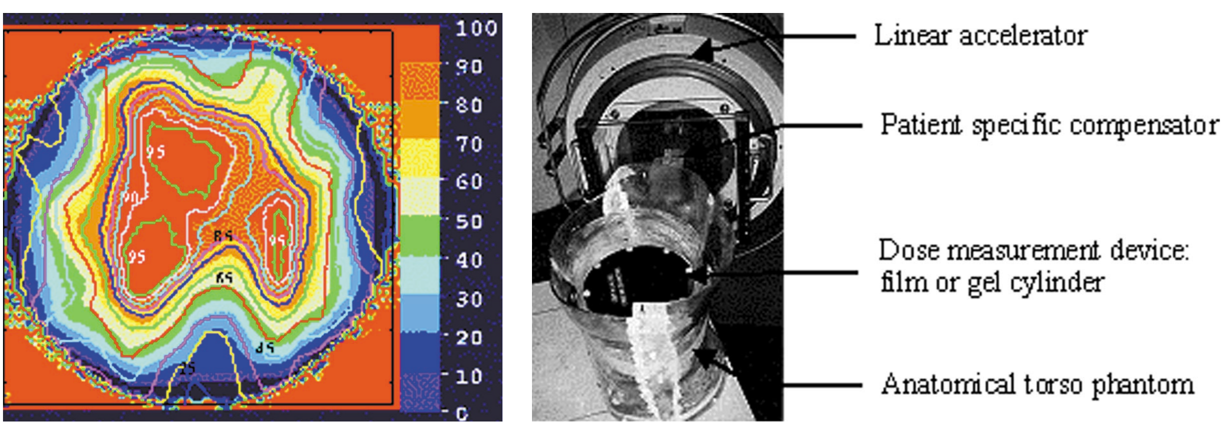
IMRT was experimentally studied for pelvic cancer treatment using two different phantoms. The first phantom was composed of cylindrical cardboard slices and between each slice a radiosensitive film was inserted. The images obtained on the films showed transverse dose distributions. A pelvic phantom constructed of Perspex was manufactured to be able to compare film dosimetry with gel dosimetry, Figure 4. The gel dosimeter used is termed BANG gel: bis-acrylamide co-polymer (4%) polymer acrylamide (4%), gelatine (5%), with nitrogen used to remove oxygen.

Head and neck phantom for gel dosimetry

A head and neck phantom in Barex™ [21] was build to test IMRT for head and neck [22], Figure 5. This phantom contains a number of tubes, which are termed *chambers*, that can be filled with various substances and sealed. A partition between the head and the neck region was attached in order to ensure that the chambers were of a reasonable size and thus minimised the amount of gel required. Valves are attached to each chamber to allow filling and draining of liquids [20, 22].

Experimental results

This section describes the ability of the imaging software to delineate ROIs and describes the experimental results undertaken to verify the accuracy of compensators and MLCs to produce optimised IBM.



a) b)

Figure 4. [a] IMRT isodose distribution obtained with film dosimetry overlaid on the MR image of the bis-acrylamide-nitrogen and gelatine (bang) gel also used to measure the radiation dose delivered to the PTV and adjacent tissues. [b] Compensator + linear accelerator based IMRT set-up used for the experimental measurements

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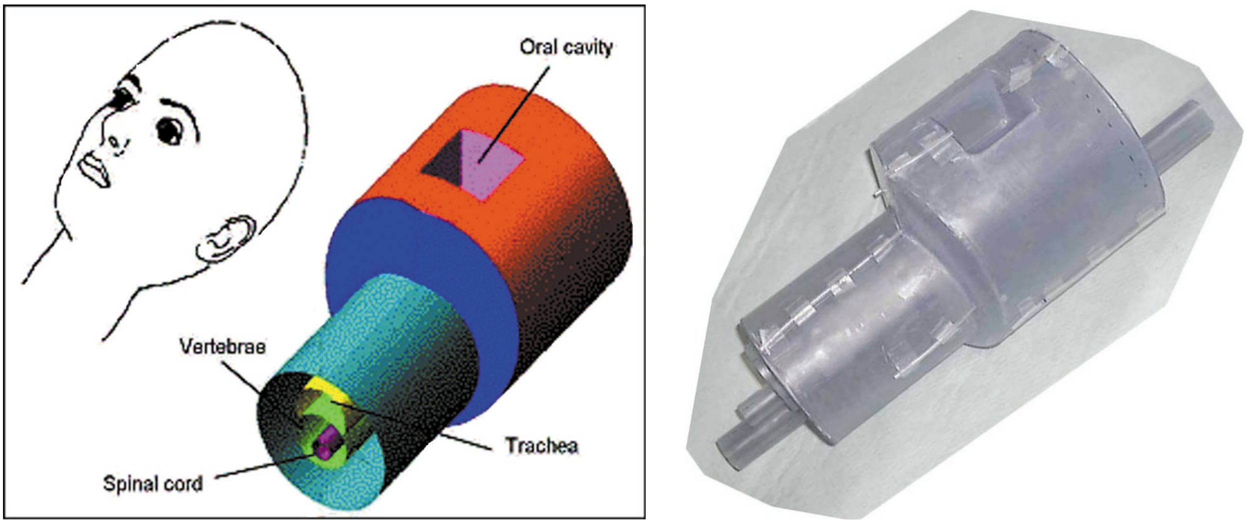


a) **b)**

Figure 5. [a] Schematic of the head and neck phantom. [b] Photograph of the phantom

Image processing

The software interface and resulting automatic delineation is illustrated in Figure 6 [12]. The advantages of the hybrid approach, Table I, include improved ability to define closed contours to separate ROIs previously joined by the growing process and to minimise the loss of structures. The original experimental system for image analysis and delineation of ROIs was based around a graphical user interface designed to facilitate the interaction with clinicians. It included image pre-processing, image segmentation and image post-processing tools as well as various editing and zooming tools.

Using the feedback rule-base method, Table II, which was developed within the Matlab environment it was shown that it was possible to differentiate between the bladder and the seminal vesicle. Such differentiation is difficult because there is very little difference in terms of grey level between the bladder and the seminal vesicles and therefore the results emphasise the value of this method.

Optimisation of IMRT

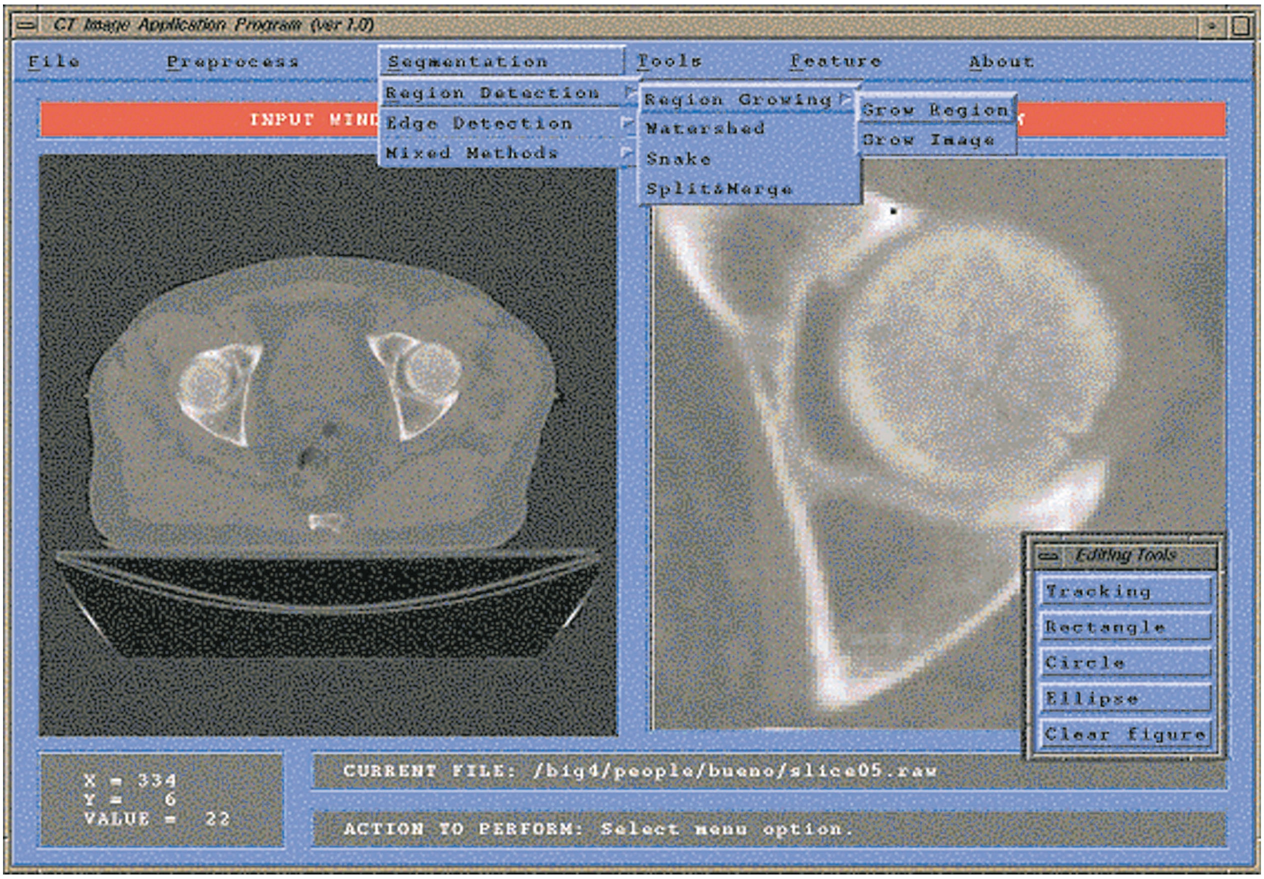
The ability of the beam orientation algorithm combined with the beam modulation software to produce a conformal dose distribution has been demonstrated. For more than five coplanar beams, it was found that in the treatment locations considered (pelvis and head & neck) equally spaced beams were preferred as they were close to being optimal and were more practical to implement than other beam arrangements. However, in the recent work of Pugachev et al [23] these authors state, that "the sensitivity of an IMRT treatment plan with respect to the selection of beam orientations varies from site to site. For some cases, the choice of beam orientations is important even when the number of beams is as large as nine. Non-coplanar beams provide an additional degree of freedom for IMRT treatment optimisation and may allow for notable improvement in the quality of some complicated plans".

Research on the optimal number of beams was also studied using a geometrical objective function. It was found that the greater the number of beams, the easier it is to comply with complex dose distributions [4]. However, as the number of beam increases, so does the treatment complexity and potential risk of errors. Therefore, for most treatments, there may not be any practical benefits in using more than 5 to 9 beams.

Figure 7 illustrates the ability of the beam modulation algorithm to produce a conformal dose distribution delivering a high uniform dose over a concave PTV and a low dose to a ROI adjacent to the concave boundary of the PTV. This IMRT plan takes into account constraints arising from the compensator manufacturing process and the couch design. It demonstrates that although the achievable resolution was reduced by the number of constraints which had to be taken into account, the resulting plan was still satisfactory. It was also superior to traditional treatment plans in terms of dose distribution [19, 20].

Dosimetric verification of IMRT plans

It has been proven for IMRT using film and gel dosimetry that it is possible to deliver a conformal dose distribution using five beams optimised in terms of position and modulation. Moreover, there is good agreement between the dose distribution obtained with film and gel dosimetry, Figure 4a. However, some discrepancies are observed between theoretical and measured dose distribution and this emphasised the need to take into consideration the compensator manufacturing process. This is because part of the beam profile could not be produced accurately due to the limitation of the milling machine used to manufacture the compensators.



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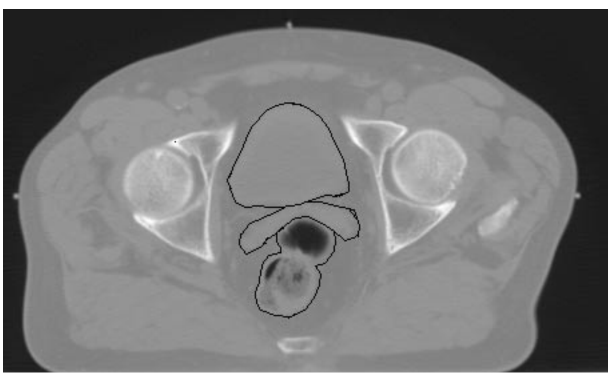

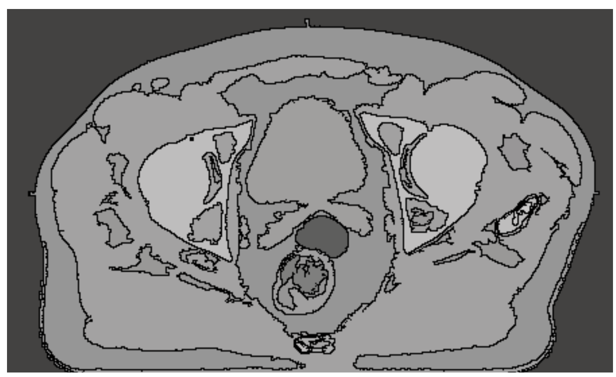

b) **c)**

Figure 6. [a] Graphical user interface of the imaging system. [b] Manual outlining of structures by a clinician. [c] Automatic outlining of structures using the workstation

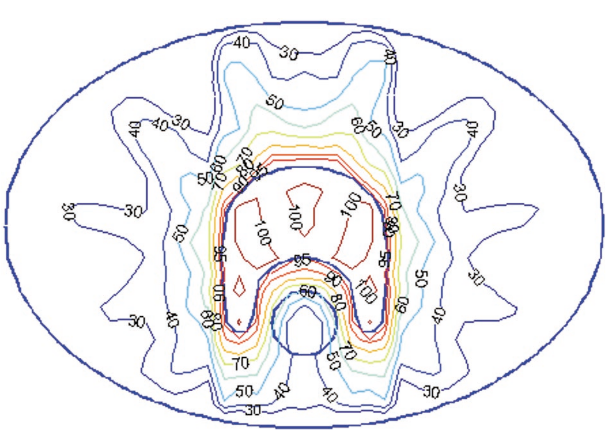

Figure 7. IMRT optimised treatment plan

Experimental limitations

Several practical limitations for experimental dosimetry for IMRT have been identified [20], Table V. The resolution achievable using compensators depends on the direction of the machining cut and the cutting direction should therefore be that of the highest modulation.

Similar results were obtained for MLCs, which can achieve a good resolution in the direction of the leafmovement, but can also give rise to unacceptable errors in the lateral direction. To overcome this problem manufacturers are designing MLCs with *thinner* leaves

Table V. Experimental limitations

– To minimise the likelihood of tool break and provide sufficient attenuation the maximum thickness is limited to 6 cm with a minimum thickness of 0.1 cm.
– The minimum and maximum height of the compensator constrained the normalised intensity modulated beam [IMB] to be larger than 0.17 and smaller than 0.97: assuming a non-attenuated IMB is equal to 1.00.
– The maximum compensator slopes in the lateral direction are 61° and 37° for *oblique* and *valley* features respectively, and 50° for a *valley* feature in the longitudinal direction. Minimum width *valleys* are implemented by forcing *peaks* and *valleys* to be at least two pencil beams width. In addition, very steep changes between neighbouring IMB profiles are prohibited.
– Smoothing filter wedge constraints force the IMB to take the form of a standard wedge, or a polynomial fit of various orders. This is to make sure that the profile produced is both smooth and continuous.

to provide higher resolution, or adopting software solutions to overcome the hardware limitations.

Conclusions

Successful introduction of modern IMRT techniques is improved by the availability of automation of both diagnostic imaging and treatment planning procedures. Based on a medical image segmentation system, *intelligent* software that exploits the clinical experience of radiation oncologists as well as information from the medical images is essential and the workstation described is of significant assistance. It should, though, be regarded as a starting point, with research and development continuing.

The method is not only applicable to IMRT optimization delivered using photon beams from linear accelerators or proton beams, but can also be used with other treatment machines such as the new total body irradiation treatment machine currently being developed at the University Hospitals Coventry and Warwickshire NHS Trust in collaboration with the Control Theory and Applications Centre of Coventry University and JME Ltd [24-27].

It is also noted that the use of multiple objective evolutionary algorithms, including MOGA, is not limited to external beam IMRT but has also been used in the field of high dose rate (HDR) brachytherapy [28, 29]. Indeed, the SWIFT real-time HDR prostate planning system developed in [28, 29] is the first commercial product where the planning is performed using a *true* multiple objective approach.

Multiple objective evolutionary algorithms offer a flexible approach to IMRT planning, being able to combine objectives in terms of dose distribution and tumour control probability within a single algorithm. It is therefore surprising that most radiotherapy treatment planning software developed to date only uses some types of weighted sum approach that provide a single solution. These software provide a single solution, that may not be clinically appropriate depending on the criteria employed.

In addition, with the increased performance of computer systems, the relative *slowness* of MOGA compared to *fast* deterministic techniques such as gradient descent methods is becoming less of an issue. The key to the approach is the ability of MOGA to provide several solutions, all of them optimal depending on the relative importance of the objectives.

This is a *one-stop-suits-all* algorithm, which is able to cater for a wide range of treatment situations (palliative and curative), treatment locations and patient conditions, without having to change a set of importance factors. Instead, clinicians could select a set of preferences, expressed using words or expressions, which a decision maker would then interpret to provide the clinician with two to three alternative solutions from the set of optimal solutions.

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'Evolutionary algorithm is an umbrella term used to describe computer-based problem solving systems, which use computational models of some of the known mechanisms of evolution as key elements in their design and implementation' [30]. A genetic algorithm is an evolutionary algorithm.

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