Radiotherapy, hadrontherapy and the treatment planning for heavy ion and proton irradiation.

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Abstract. The aim of conformal radiation therapy is to deliver the dose as high and as uniform as possible to diseased tissue sparing all the other parts, without causing unwanted and unnecessary side effects for the patient. Difficulties to achieve this goal start with the determination of the three-dimensional volumes of interest and end up in realizing a three-dimensional uniform and maximal as possible, the dose distribution. The technique of intensity-modulated radiotherapy (IMRT) as form of conformation in radiation therapy is a real revolution. One of the newest attempts in this field, which reaches to have a great success, is the use of multi-leaf collimators (MLC). It is not the unique new technique. In fact the use of therapeutic ions, especially carbon ions and protons is the technology of the actual future which is really the challenge in conformation of dose to targets, thanks to energy deposition characteristics of hadronic beams.

An appropriate treatment planning system is strictly necessary to take full advantage of the novel technique. We have developed, for this purpose, an analytical code in C++ language, running on Unix platform.

The package presented, is a special code system dedicated to the planning of radiotherapy with energetic ions. ANCOD is an analytical code using the voxel-scan technique as an active method for irradiating the patients. It is based on an iterative algorithm to determine the best fluencies to realize the optimal dose distribution, delivering a maximum of dose on the target volume and a minimum of dose distribution all around, especially on organs at risk.

As input, the code use experimental data of linear energy-loss of a particular set of initial kinetic energies, and as a clinical data a complete set of CT images with contours of volumes of interest.

Inverse planning techniques are implemented in order to obtain the initial energies needed for each beam to have a uniform target dose distribution.

The package can determine the fluencies and energies of several thousand of pencil beams in few minutes. The performances of the program are tested with a full simulation.

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I. **Radiotherapy as a solution to cancer.**

![Diagram showing statistics on cancer and different treatments used in Europe.](image)

**Figure 1** Statistics on cancer and different treatment used in Europe.

Radiotherapy is the most widely form of cancer treatment, with treatment given to two out of every three patients. It is involved in almost half of curative cancer treatments. Radiotherapy allows organ preservation (e.g., breast, eye, larynx, extremities) in up to 40% of curable patients, thus having also a significant impact on an improved quality of life.

In fact, early statistics showed that 5% of patient with generalized cancer was successful treated with chemotherapy. In case of localized cancer and before any metastasis the chance to definitively cure the patient increases considerably. Indeed, 40% of treatments are successful in 22% of cases thanks to surgery. Radiotherapy has the privilege to cure the rest of the cases or at least in combined to surgery or chemotherapy!

In radiation oncology departments, the standard equipment for radiotherapy consists of $^{60}$Co units and of linear accelerators with different photon energies (and also with variable electron energies up to 25 Mev).

The radiotherapy aims to achieve a high therapeutic ratio, defined as the ratio of the probability of tumour control and the probability of normal tissue complication. Ways to do this with x-rays rely on arranging that the dose to organs-at-risks significantly lower then the dose to the target volume by suitable multiport with different kinds of techniques, including those involving shaping the geometric field to the beam's-eye-view of the target, whose ultimate aim is dose conformation to the target volume.
II. **Radiotherapy, the history.**

Let’s start the story from the beginning, which is the diagnostic of cancer. Tools used initially for that purpose was really primitive comparing with the big progress done in the field of medical imaging now. Since the simple radiographic devices till the PET and MRI scanners there was a very accurate and long work of multidiscipline experts. The planning of the treatment was conventionally done considering always a rectangularly shaped field steered to a target volume estimated just from planar radiographs and in general just the central one. This was making the margin of errors larger and larger.

Since the advent of computerized tomography (CT) around 1972, the error margin starts to be reduced. The tumour was better defined and the quality of images can provide more precise information about the volume to be treated. However, the planning was made in a single axial slice. This was however an other source of errors since the central slice is not all the time the only one we should consider.

The era of three-dimensional planning started from a necessity and with the opportunity to have a big variety of medical imaging devices and technologies. It is true that the mathematical models for a three-dimension reconstruction are a bit complicated when try to approach the real 3-D volume but very powerful algorithms were developed with a high precision.

The concept of conformal irradiation was introduced by Busse and Friedman et al. in the 1950s and Proimos and Takahashi et al. in the early 1960s. With the advent of 3D treatment planning and looking to make a better conformation in radiotherapy, different techniques and notions were developed. Initially they used just blocks, compensators and bolus designed in such way to conform better the dose to the target based on the concept of Beam’s Eye View (BEV) which had and still has a great contribution to the conformal radiotherapy. Then more complicated techniques were developed. Intensity Modulated Radiotherapy (IMRT) involves now the newest technologies to the conformation using new accessory more precise and giving the possibility to take advantage from the free parameters we can have.

In fact, IMRT allows a single accelerator beam to function as if it were many much smaller beams each of which can be controlled individually. Intensity modulated beams can be produced directly by the accelerator itself or through the use of collimator which modulates the beam emitted by the accelerator. With the advent of the multileaf collimator (MLC) more convenient geometric field shaping could be engineered (see figure 2 ).
Progress was realized cancelling all conventions and studying every detail to be more precise reducing possibility of errors and therefore improving the quality of the treatment. The optimization techniques in radiotherapy, like in all fields looking for precision, allow avoiding random attempts to approach the right one.

III. Hadrontherapy and its particularities.

The use of beams of protons and heavy ions instead electrons or photons born when the characteristic of Bragg peak showed a great advantage in the way to deposit the energy.

In fact, when an energetic heavy charged particle penetrates matter it is slowed down mainly by numerous ionizing collisions with the atomic electrons of the medium. The probability for such collisions increases with decreasing particle energy. Therefore ion beams loose a large fraction of their initial kinetic energy in a relatively narrow region at the end of their path the so-called Bragg peak. The dose deposition in the entrance channel is relatively low (see figure 3).

Figure 2: Multi leaf Collimator one of the more advanced accessory largely used now as a new technique to conform the dose in intensity modulated radiotherapy (IMRT).

Figure 3: Comparison of the depth dose profiles of photon, electron and carbon-ion beams.
Principally, the radiobiological as well as physical factors determine local tumour control in radiation oncology. Both factors enter into the differential between tumour and normal tissue responses. While radiobiological factors generally aim for relatively greater damage in tumours with equal radiation dose, physical factors make it possible to give higher doses to the tumour than to the surrounding healthy tissues (high precision radiotherapy with superior dose distribution and good selectivity). Heavy ions making much more damages in the DNA structure decrease the probability of cell survival (see figure 4).

**Figure 4** Calculated tracks respectively of photons, protons, α-particles and carbon ions compared with the dimensions of a schematic view of a DNA molecule.

The Relative Biological Efficiency (RBE) was defined as the ratio of photon dose $D_\gamma$ to the particle dose $D$ leading to the same biological effect. It helps to see clearly the
advantage of heavy ions on the conventional photons or electrons and it is an important factor in field of hadrontherapy especially when talking about biological optimization.

**IV. Treatment planning in hadrontherapy.**

Computers have been used in planning radiation therapy over a time period approaching 40 years.

However, the progress in computer hardware and software seen during the last decade have led to the development of sophisticated three-dimensional radiation treatment planning (3DRT) systems and treatment delivery systems which have made practical the implementation of three-dimensional conformal radiation therapy (3DRT)

The first 3D approach to RTP (dose calculation and display) is credited to Sterling et al. who demonstrated a technique by which a computer generated a film loop gave the illusion of a 3D view of the relevant anatomical features and the calculated isodose distribution throughout a treatment volume.

The advantage of 3DCRT and the use of BEV display beam was quickly grasped by several groups, and contributes greatly in the development of more powerful 3DRT systems.

Advanced planning provides more sophisticated software tools such as dose volume histograms (DVHs) and biological indices.

A three-dimensional treatment planning requires a computer with a large storage capacity for 3D images and for dose distributions. Should preferably, also, support high quality graphical display to provide a good enough 3D view.

The treatment planning systems (TPS) used in radiotherapy are so many that could be boring to try even general description in this paper. Therefore, starting from the end of the experience in radiotherapy TPS, I will describe one of the few codes dedicated particularly to 3-D treatment planning for hadrons therapy. It is an ANalytical CODE (ANCOD) for just protons and heavy charged particles, which was implemented at the beginning in Fortran programming language and now converted to C++.

ANCOD is based on two assumptions:

- The dose delivery system is done in elementary steps. At each step one voxel of the target is irradiated. It is the active method of dose delivering called spot scanning technique.
- The beams, composing each field, are described as a mono-energetic pencil beam aiming at the voxel centre and the energy is computed so as to have the Bragg peak right in the centre of the voxel.

The task of finding the optimal plan is shared between the reading part, the treatment part and the output part.

The first part makes the necessary step to provide all necessary information about the patient and the data base of the charged particle used.
The second part starts making the intermediate operations before the real optimization. There is the extraction of energies needed for each pencil beam and calculation of linear energy deposited by each pencil beam in each elementary volume (voxel) crossed during a given treatment plan, then comes the optimization to find the best set of fluence values of the pencil beams to realize a maximal dose, uniformly distributed on the target volume and a minimum dose all around sparing in this way the organs at risk. The inverse planning algorithm used is based on an iterative approach repeated till a given tolerance.

The runtime with the new C++ version of the code is excellent and contrary to simulation codes needs just few minutes to find the optimal parameterizations for a given planning, particularly the best fluences set and the right energies of each of the pencil beams. As seen in the two figures 5-6, our requirements are well satisfied and we reached with a high accuracy to conform the dose to the target and not just considering one central slice but all the other slices as well, so we reached to make really a three-dimensional physical optimization.

![Dose Distribution Diagram](image)

**Figure 5** Example of dose distribution in a central slice of the cranial part.
but then the expenses decrease quickly.

It adopts the newest techniques of treatment planning, optimizing time and in that way the optimization values of fluences.

**Conclusion.**

Hadrontherapy has a big chance to be the therapy of the future since it has really minimum possible side effects, sparing as no other technique can do the organs at risk. It adopts the newest techniques of treatment planning, optimizing time and in that way money also. It is now a technique a bit expensive comparing with therapies with photon or electrons but like all the new technologies at the beginning the precision costs a lot but then the expenses decrease quickly.

**REFERENCES**


