Optimization of Cancer Treatment with Accelerator Produced Radiations.

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1. Introduction

About 30 years ago large particle accelerators were built for tumor therapy. A successful therapy of deep situated tumors was initiated with three main advantages, which will be discussed in chapter 2. This is now considered being standard technique in radiotherapy and must be present in any new modality at least at the level obtained already.

During the past decades important progress was achieved in tumor diagnosis and in tumor radiobiology (chapter 3). This will be taken into account in the construction and optimization of a new generation of medical accelarators for tumor therapy (chapter 4).

2. Advantages of high energy photons and electrons.

2.1 Depth dose distribution

In general, the radiation beam used for radiotherapy should allow to irradiate the whole tumor with a homogeneous dose. Normal tissue in front of the tumor and behind the tumor should receive only a very small dose. With conventional X-rays a dose can be obtained in 5 cm depth in tissue, which is about 0.5 of the surface dose as shown in fig.1. This value can be increased to about 0.7 if cobalt gamma rays are used. High energy photons from particle accelerators, however, produce a dose which increases up to a depth corresponding to the mean range of the electrons produced by this photon spectrum. High energy electrons show a depth dose-curve, which is more or less constant over several cm and then decreases due to slowing down, scattering and straggling.

In most treatment cases many beam directions are used with the beams crossing in the tumor region. The beams from accelerators therefore allow to spare the normal tissue in front of the tumor (photons) or behind the tumor (electrons) in a much better way than can be achieved with conventional X-rays or gamma rays. They are, however, not optimal in this respect as will be shown later.

2.2 Influence of inhomogeneities

Conventional X-rays are absorbed in matter mainly due to the photo effect, which strongly depends on the atomic number Z. Therefore inhomogeneities in the tissue such as bones throw a "shadow" onto the tumor to be irradiated. This shadow area of low dose could be the origin for later regrowth of the tumor. In contrast, high energy photons are absorbed mainly by Compton effects which are much less dependent on Z and as a consequence this influence of inhomogeneities can be neglected. In treatment planning for electron beams the density of the different tissues is of influence on the contours of isodose lines. This has to be considered in special treatment cases.

2.3 Radiation scattered out of the beam

The most important advantage of high energy radiations in tumor therapy is the reduced scattering angle. With conventional X-rays the whole body of the patient gets a considerable dose from radiation scattered out of the tumor target region, causing radiation illness of the patient combined with vomiting and nausea. With high energy photons and electrons these side effects are reduced drastically leading to a much better health condition of the patient during treatment.

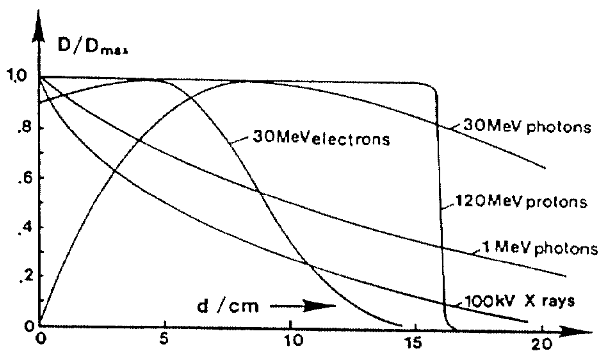

Fig. 1 Relative dose D/D_{max} as a function of depth in tissue for different types of radiations used in radiotherapy.

3. Improvements in tumor diagnosis

3.1 Shape of the tumor

In many therapeutic cases radiosensitive organs are very close to the tumor and may therefore receive a considerably high radiation dose. Radiation reactions in these organs may limit the maximum dose to be given to the tumor and in this way decide on the overall result of the therapy.

The type of radiation used in therapy should therefore allow to irradiate mainly the tumor and to spare the surrounding normal tissue. The high energy radiations used till now are not optimal in this respect. Since some years the three dimensional shape of the tumor can be determined precisely with the help of X-ray computer tomography. In three dimensional treatment planning with particle beams these data can be used now for effective sparing of neighboured radiosensitive organs as will be explained later in detail.

3.2 Properties of tumor tissue

Different functions of tumor tissue can be detected, e.g. also in pictures taken with nuclear magnetic resonance signals (NMR). Especially tumor cells with invasive growth into the normal tissue can be distinguished from resting hypoxic or necrotic cells in the inner parts of the tumor. Treatment planning should take into consideration these different functions of tumor tissues.

3.3 Radiobiology of tumor destruction.

Experiments with animal tumors have shown that tumor growth results in different types of tumor cells in relation to their supply with oxygen and nutrients. Irradiation of a tumor with many dose fractions therefore destroys first an outer shell of radiosensitive euoxic tumor cells. An inner shell consists of hypoxic tumor cells which are less radiosensitive by a factor of about two. These cells are sufficiently supplied with nutrients and are able to repair most of the radiation lesions. These cells are reoxigenated until the next irradiation takes place and are therefore mainly destroyed by the second irradiation, leaving vital again a more central shell of hypoxic cells with high repair capacity. In this way the tumor seems to be destroyed, progressing with each dose fraction from outer shells to the central region.

Only few experimental data exist for the final destruction of radiation inactivated cells and the transportation of debris material from the tumor region through the normal tissue by the host organism. These important actions should also be considered in an optimal treatment planning of the dose distribution in the tumor as well as in the temporal schedule of application of the dose fractions.

3.4 Inhibition of repair in tumor cells.

The radiation sensitivity of a tumor can be increased by selective inhibition of repair of radiation damage in tumor cells. As explained in 3.3 a most radioresistant shell of cells exists in the tumor which may influence mainly its overall radio-sensitivity. From animal experiments it is known that repair in hypoxic tumor cells can be inhibited by antimetabolites of the glycolytic energy metabolism. In this way the radiation sensitivity of the tumor can be increased without causing similar reaction in the euoxic normal tissue.

All these important improvements have an impact on the design of an optimal medical accelerator facility for tumor therapy.

4. Optimal medical accelerator for tumor therapy.

4.1 Choice of radiation type.

Sparsely ionizing radiation can be produced unexpensively with high dose rate and therefore should be used for tumor therapy. Most of the produced radiation lesions in the cells then are reparable and optimal sparing of normal tissue can be achieved. Radiation sensitivity in the tumor, on the other hand, can be increased selectively by antimetabolites as explained in 3.4.

A steep dose reduction at the edge of the tumor within few millimeter should be achievable to irradiate the tumor with a high dose in its three dimensional contour and to spare normal tissue completely in the near vicinity. Protons seem to be optimal for this purpose since scattering and energy straggling in matter is sufficiently low. A maximum energy of 250 MeV is sufficient for access of all types of tumors in different shaped patients.

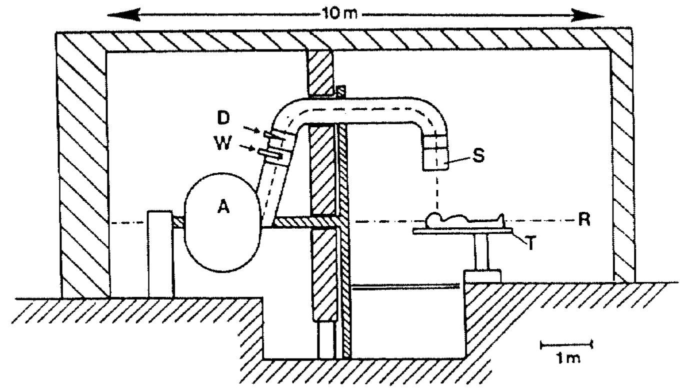

Fig. 2 Scheme of proton tumor therapy facility.
A: Accelerator with superconducting coils;
D: Energy degrader; W: Energy wobbler;
R: Rotation axis; S: Beam scanning system;
T: Treatment table.

4.2 Choice of accelerator.

For optimal treatment planning it is essential that isocentric beams from every direction are available. This can be achieved either by moving only the beam transmission system or by movement of the whole accelerator system. The latter is possible only if the accelerator is not too bulky. In many hospitals old large betatrons or linear accelerators are in operation which have to be exchanged in the next years. It will reduce the overall expenses considerably if these rooms can be used in future for proton therapy. Therefore in fig.2 a sketch of a superconducting proton accelerator is drawn with the beam transmission system and the treatment table for the patient. Treatment field sizes of about 20 cm diameter can be obtained by scanning the proton beam with magnetic lenses.

4.3 Dynamic treatment.

The knowledge of the threedimensional contour of the tumor allows to scan the proton beam in accordance with this shape as indicated in fig.3. The tumor is irradiated first from direction (a) with a scanning beam of about 5 mm diameter. The energy of the protons is changed continuously during scanning with the help of a movable absorber in the beam (fig.2,(D)) to follow the contour of the tumor. The other beam directions (b) to (d) are chosen for further dose fractions to spare totally the normal tissue in a certain radiosensitive organ (fig.3 (S)).

4.4 Variable edge treatment.

Due to the small particle scattering and small energy straggling of the protons a sharp decrease of dose within few millimeters can be achieved at a depth in tissue corresponding to the range of the particle. For the dynamic treatment mode as explained in 4.3 the diameter of the scanning beam should be around 5 mm. This steep dose decrease will be used in those sectors of the tumor where radiosensitive organs are neighboured.

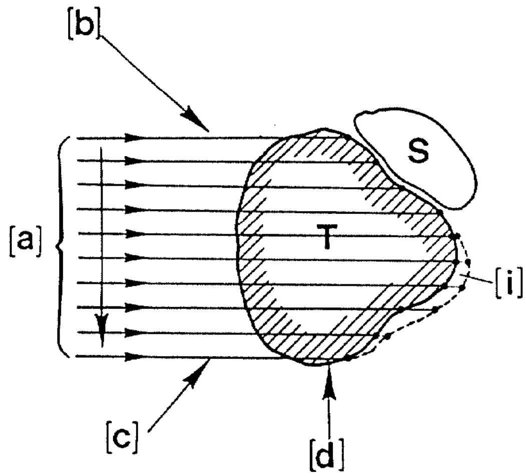

Fig. 3 Scheme of dynamic treatment of three-dimensional shaped tumors. (a): Beam direction during beam scanning for one dose fraction; (b) to (d): Beam directions used for further dose fractions; (s): region of radiosensitive organs; (i): region of infiltrative growth ot the tumor.

In regions with infiltrative growth of the tumor into the normal tissue a shallow decrease of dose must be provided with the 50% isodose line at the maximum edge of infiltration. This can be achieved best by wobbling the range of the original beam in this area. For this purpose a fast revolving wheel with sawtooth shaped absorber material can be moved into the beam as indicated in fig.3 (W).

4.5 Application of adjuvant measures.

As explained in 3.4 adjuvant drugs can be applied for increasing the radiation sensitivity of the tumor. Such a treatment has to be done about one hour before irradiation but lasts only several minutes.Rooms for this treatment of the patients should be available therefore in the vicinity of the accelerator faciliy.

For high precision irradiation of a tumor it is essential to provide precise positioning and fixation of the patient on the treatment table. This will need some minutes if done carefully and with comfort for the patient. A high number of patients can be treated per day (about 100 to 200) if two preparation rooms with beam simulators can be used alternatively.

5. Summary

A small superconducting proton accelerator seems to be an optimal device for advanced modern radiotherapy of deep situated tumors to be treated in a large number of hospitals. New irradiation techniques and irradiation modalities achievable with such installations can make use of the progress in tumor diagnosis as well as in tumor radiobiology.