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STEREOTACTIC RADIOTHERAPY OF MALIGNANCIES IN THE ABDOMEN

Methodological aspects

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A method for sterotactic high-dose radiotherapy of malignancies in the abdomen has been developed. A stereotactic frame for the body has been developed and a method for fixation of the patient in the frame is described. The reproducibility in the stereotactic system of tumours in the liver and the lung was found to be within 5–8 mm for 90% of the patient set-ups. The diaphragmatic movements were reduced to 5–10 mm, by applying a pressure on the abdomen. An analytical method is used to calculate dose distributions for a continuum of beams in an isocentric treatment technique. The advantage of a heterogeneous target dose is demonstrated and proposed for the present application. A non-coplanar treatment technique, using eight individually shaped beams is proposed and has been used for patient treatments. The dose distribution for a patient with a metastasis in the liver is shown as well as dose volume histograms for the target and the liver.

At the Karolinska Hospital non-malignant and primary malignant intracranial targets have been treated with radiosurgery using the 'gamma knife' since 1974. During recent years brain metastases have also been treated in several hundreds of patients. The treatment is given as a single irradiation of the target without any margin to the extension seen on CT. A prerequisite for this method is the sterotactic system used for localization and for patient set-up. The rigid connection between the stereotactic frame and the head is obtained by screws from the frame to the skull.

The experience of tissue tolerance to localized single fraction high-dose radiotherapy stems from the early application of radiation therapy and more recently from radiosurgery for intracranial targets and intraoperative radiotherapy (IORT) for extracranial targets. In radiosurgery the target volume is generally in the order of from a few cm^3 up to about 20 cm^3 and the dose distribution within the target is generally very heterogeneous. The minimum dose in the target ranges from 10 to 30 Gy, and the maximum dose is about twice as high. In IORT a volume of up to several hundred cm^3 receives a single dose of up to 30 Gy. A considerable part of this volume may contain normal tissue.

The experience of the radiation tolerance of tissues in the abdomen from IORT coupled with the positive results of radiosurgical treatment of intracranial lesions makes it attractive to investigate a method for stereotactic external beam radiotherapy of small localized targets in the abdomen. The basic problem of such a technique is the fixation of the patient for accurate beam set-up, and the sterotactic localization of the target. The method here described is intended for a small number of high-dose fractions.

A new method is described for stereotactic localization and fixation of target volumes for the treatment of malignancies in the abdomen. Furthermore, a theoretical study is presented concerning dose distributions that can be achieved by different irradiation geometries by an isocentric technique. The method has been studied for treatment of tumors in the liver. Liver tumors were chosen for two main reasons. Firstly, conventional fractionated radiotherapy has not been successful, because of the low radiation tolerance of normal liver tissue [1]. Secondly, the liver is a

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large organ with a considerable spare capacity. This means that even a relatively large part of the normal liver can be inactivated by irradiation without hazardizing the health of the patient [2, 3]. The method presented has been used in clinical practice for more than two years and the present report will concentrate on the methodological aspects.

Material and Methods

Stereotactic body frame. A stereotactic frame for the body has been developed. The size and shape of the frame was chosen to fit CT-, MR- and PET scanners with an aperture of at least 55 cm. The materials in the frame are wood and plastic to give a minimum of artefacts in the above mentioned tomographic diagnostic images. Fig. 1 shows a schematic view of the stereotactic body frame and how the patient is positioned. The support of the patient is obtained by a means of a vacuum pillow. The length of the vacuum pillow extends from the head to the thighs. The walls of the frame thus serve as a support of the vacuum pillow. In this application a very large contact area between the soft tissue of the patient and the frame is used to obtain a reproducible position of the patient. This is contrary to the principle of head frames, in which a small contact area between the bony structures of the skull and the frame is used. Since the walls of the body frame are made of wood it is possible to irradiate through them with only a small attenuation of the beam, which can be corrected for. The stereotactic system of the frame, visible on the tomographic slices, consists of indicators on the inside of the frame (Fig. 1). The longitudinal scale is 800 mm in length. The construction of this scale (Fig. 2) consists of seven indicators (A), on which multiples of 100 mm can be read. There are furthermore eight 45° indicators, each of 100 mm length (B). A reading of 634 mm on the longtiudinal scale is illustrated in Fig. 2.

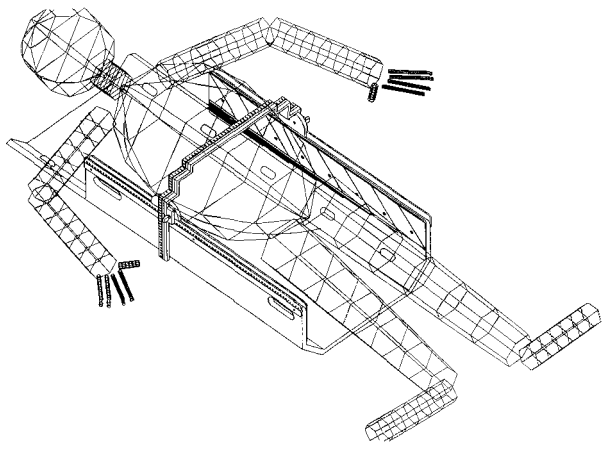


Fig. 1. Schematic view of the sterotactic body frame and the position of the patient in the frame.

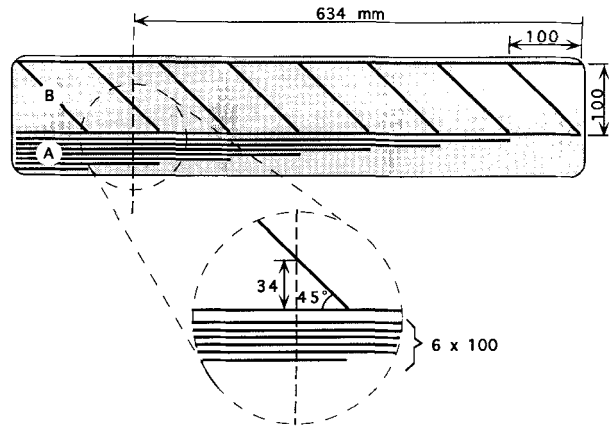


Fig. 2. The construction of the longitudinal CT scale.

For correct isocenter positioning in the treatment room, scales on the outside of the frame are used (Fig. 1). The bow over the patient (Fig. 1) is a ruler that can slide back and forth. This ruler is used in the treatment room to determine the correct set-up in the transversal plane. The room-mounted lasers, which indicate the isocenter of the treatment unit, are used for the set-up. At local high-dose treatment of malignancies in the liver the diaphragmatic movements should be minimized. These movements, which were examined on 17 patients by fluoroscopy during quiet respiration, were found to range between 1.5 and 2.5 cm. By applying a slight, constant pressure on the abdomen the diaphragm was displaced in the cranial direction about 1.5 cm, and the diaphragmatic movements were reduced to 0.5–1.0 cm. This effect could be reproduced by a belt that was tightened to a certain length around the patient to ensure the same position of the liver during CT examination and the treatment. CT examination of the patient, fixed in the stereotactic frame, is made shortly before each treatment in order to study the reproducibility of the target in the stereotactic system. The reproducibility is measured in relation to the first CT examination, which is used for the dose planning. The reproducibility in the stereotactic system of targets in liver and lung was determined in 16 patients on 28 occasions. The measurements on the CT slices were facilitated by the matching function on the dose planning system (TMS, HELAX). By this function two CT studies can be compared when a transform between the two studies has been defined. The transform was in this case determined from the stereotactic frame. Selected points in one CT slice from one study are transformed to a corresponding CT slice (measured on the longtitudinal scale of the stereotactic frame) in a study performed on another occasion (see Fig. 3). The points in the left slice (first examination) have been transformed to the right slice (second examination). As can be seen in Fig. 3 the positions of the liver and the metastasis only differ by a few mm, between the two examinations which were performed one week apart.

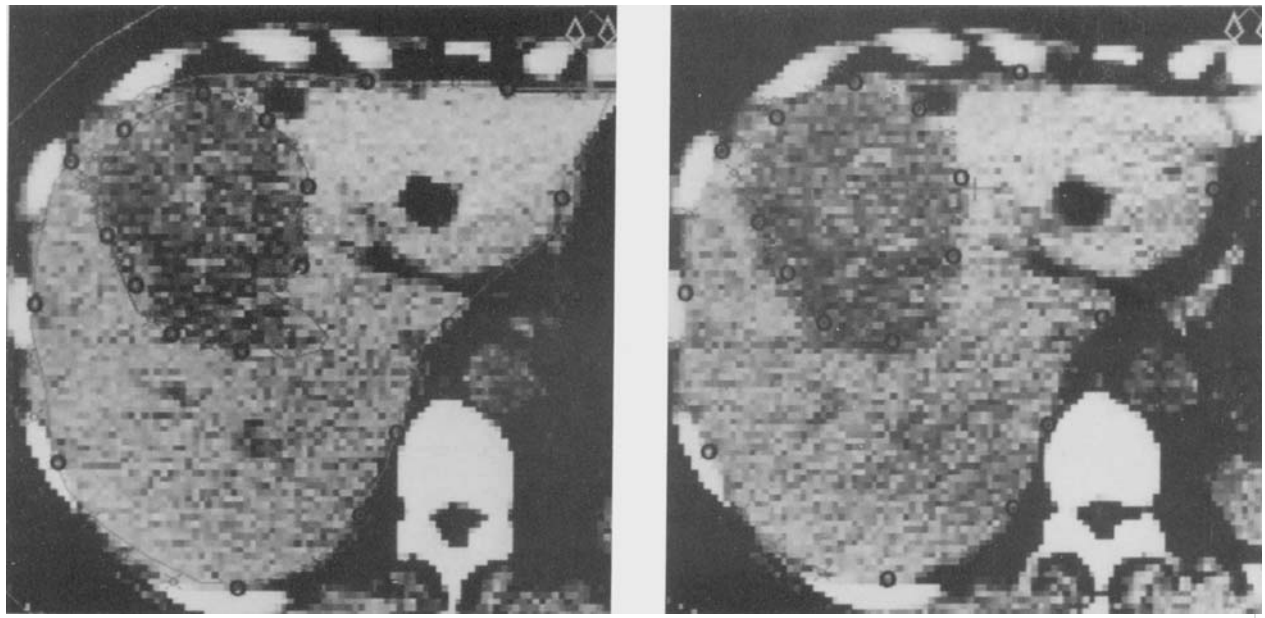


Fig. 3. Check of reproducibility. The left panel shows a study one week before treatment and the right panel a study one hour before treatment. A transform between the two studies was defined with the sterotactic system. The comparison of the two CT slices was made by defining the crosses in the left slice, that were transformed to the right slice.

Theory. The dose distribution for a continuum of beams distributed within the angular intervals (α, β ; Fig. 4) can be described with reasonable approximations by simple analytical expressions as previously reported by Lax (4) for ^{60}Co beams used in radiosurgery. By assuming a parallel beam with a lateral beam profile P(r) and an attenuation coefficient μ, the normalized dose distribution along the x axis, D(x) is given by the following expression (4)

$$D(x) = \frac{\int_{\alpha}\int_{\beta} P(r)\exp(\mu x \cos\alpha \cos\beta)\cos\beta \, d\alpha \, d\beta}{\int_{\alpha}\int_{\beta} \cos\beta \, d\alpha \, d\beta} \quad [1]$$

$$r = x((\sin\alpha)^2 + (\cos\alpha \sin\beta)^2)^{1/2} \quad [2]$$

Similarly the normalized dose distribution along the y axis, D(y), is give by

$$D(y) = \frac{\int_{\beta} P(r)\exp(\mu y \sin\beta)\cos\beta \, d\beta}{\int_{\beta} \cos\beta \, d\beta} \quad [3]$$

$$r = y \cos\beta \quad [4]$$

The expressions were derived by assuming that each beam gives the same dose contribution at the isocenter. The expressions are thus independent of the geometry of the absorbing medium. Dose distributions have been calculated for a 21 MV photon beam by numerical integration of eqs. [1] and [3]. The beam profile P(r) was taken

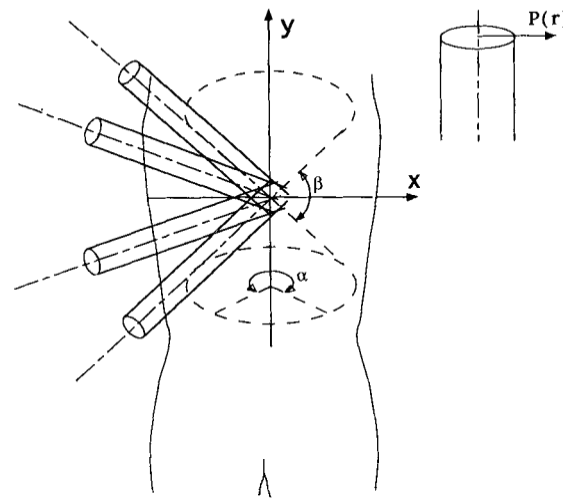


Fig. 4. Irradiation geometry. A continuum of circular beams are distributed in the angular interval α, β. The radius of the beams are R. The dose profile of the beams is given by P(r).

from experimental data for the microtron (MM22) at the Karolinska Hospital. The value of the attenuation coefficient used was 0.0467 cm^{-1}. The results of the calculations are presented by the position coordinates x and y normalized to the radius R (= 2.5 cm) of the target. This makes the results, wth good approximation, valid for beam radii between about 1.5 cm to about 4 cm, though the calculations were made for the beam radii 1.0 R, 0.9 R, and 0.8 R. The error caused by the parallel beam approximation is very small. In the above mentioned paper (4)

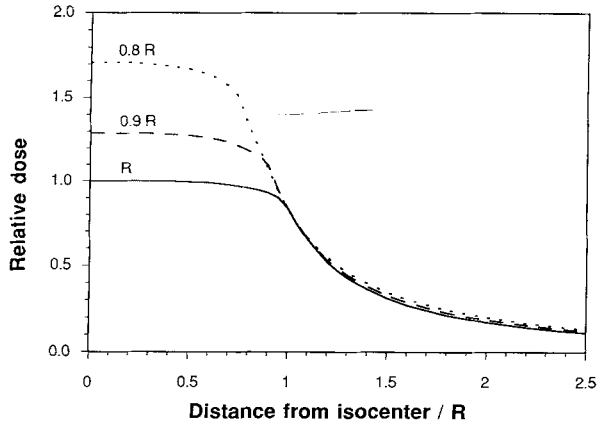


Fig. 5. Relative dose versus distance from isocenter/R. The beam radii are R = 2.5 cm, 0.9 R and 0.8 R. The calculations were made for $\alpha = 360°$ and $\beta = 180°$. The dose distributions are weighted to give the same dose at the position coordinate 1.0. For this isotropic irradiation the dose in the x and y directions will be exactly the same.

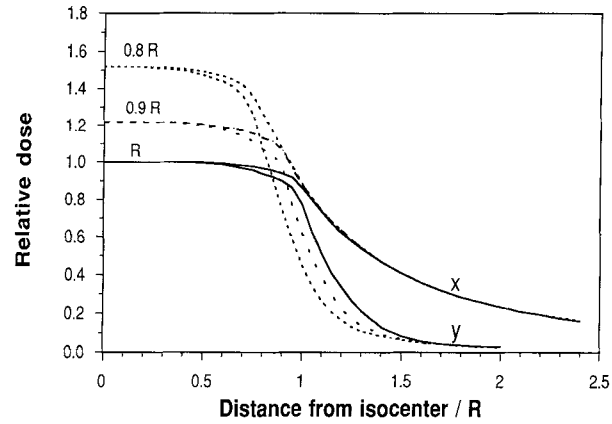


Fig. 6. Relative dose versus position x and y. The calculations were made for $\alpha = 360°$ and $\beta = 90°$.

several beam geometries were investigated for ^{60}Co beams. In the present work the impact of a highly heterogeneous target dose, on the dose outside the target, has been studied for 21 MV photon beams. In situations with lower radiosensitivity in the central parts of the target due to anoxia, improved treatment results can be expected if the dose in this region is increased while the dose in the periphery of the target is kept constant. However, to increase the therapeutic ratio the dose in the tissue surrounding the target should not be increased. Such a dose distribution can to a great extent be obtained by using beams with a radius smaller then that of the target, and with the dose distribution normalized to the periphery of the target. The present calculations were made for three beam radii; 0.8 R, 0.9 R and 1.0 R and the beam geometry was a hypothetical isotropic irradiation (4 π) with $\alpha = 360°$ and $\beta = 180°$. Fig. 5 shows that a beam radius equal to that of the target gives a fairly homogenous target dose (solid line). The results for the two smaller beam radii show that the central parts can be given a higher dose, whereas the dose in the volume outside the target is only marginally increased. This effect can be taken advantage of when several, partially overlapping, beams are used as in radiosurgery where the dose in the periphery of the target usually is in the order of 50% of the maximum dose. Calculations were also made for a more realistic beam geometry, $\alpha = 360°$ and $\beta = 90°$, with three different beam radii. Using this beam geometry the dose distributions are different in the transversal (x) and the longitudinal (y) directions. The dose distributions were weighted to give the same dose in the periphery of the target in the transversal direction. The result presented in Fig. 6 shows that the central parts can be given a considerably higher dose with only a marginal increase of the dose in the surrounding tissue. A result from this calculation is that for the more realistic beam geometries with an angle β of 90°, the beams must be elongated in the longitudinal direction to cover the target. The present calculations were made for a spherical target. However, the results regarding the dose within versus outside the target, are applicable to irregular targets as well, for beam geometries similar to the one here used. The dose outside the target will primarily depend on the dose in its periphery and to a minor extent on the dose in its central parts (4).

Dose planning. The dose distributions presented in Figs. 5 and 6 were calculated for a continuum of beams within certain angular intervals. In radiosurgery with the 'gamma knife', 201 beams are used whereas the technique with accelerators is that of multiple arcs. These techniques will, for a single isocenter, essentially produce a spherical dose distribution. For the present application is was considered important to obtain conformity of the dose distribution with the shape of the often irregular target volume. The present technique is based on a limited number of static individually shaped non-coplanar beams. For practical reasons the number of beams has to be minimized. However, a relatively small number of beams can be used to obtain dose distributions similar to that in Figs. 5 and 6, regarding the dose fall-off at the periphery of the target (5). This is especially true for the higher relative dose levels and targets with a size of about 2 cm or more (5, 6). The intention was to obtain a dose distribution similar to the one presented in Fig. 6, i.e. with a heterogeneous target dose. An isocentric non-coplanar technique with 8 individually shaped beams was evaluated. The energy of the photon beams was 21 MV. The directions of the beams were selected in order to distribute the entrance and exit rays within a large solid angle. An acceptable dose distribution was obtained by using four different coach angles. Two beams were planned for a zero degree coach angle, two beams for each of plus and minus 45° respectively and two beams for a coach angle of plus 90°. For the two beams at each of the couch angles 45°, −45° and 90° the

gantry angles were 45° and −45°. A wedge was planned for most of the beams. Individual blocks, determined by in beams eye view, were planned for all beams. However, the blocking was kept quite simple by defining blocks with straight edges to block corners of the fields. In this way it was possible to use loose blocks with a magnet fixation on the shadow tray. The blocks were positioned by means of plots of the beams eye views. The dose planning was performed with the 3D system TMS. About 40 CT slices with a spacing of 1 cm were used. The location of the isocenter was determined in the sterotactic system, using the dose planning system. The dose distribution was calculated in a three-dimensional dose matrix, and could be visualized in all the CT slices. Dose volume histograms were calculated for the target volume and for the 'host organ'.

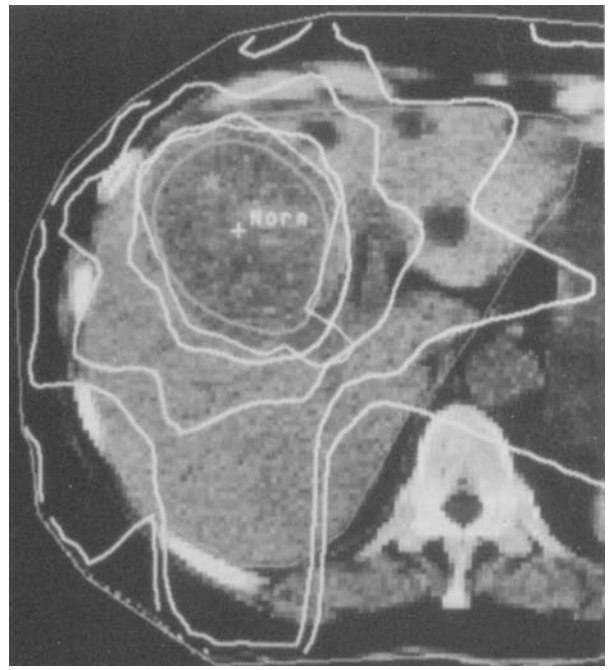
Results

The reproducibility of the target in the stereotactic system for the 28 patient examinations mentioned above is presented in the Table with the deviation of the target position given in relation to the first CT examination. The deviation is given in scalar units, i.e. without regard to the direction of the deviation. There was no systematic deviation in any direction.

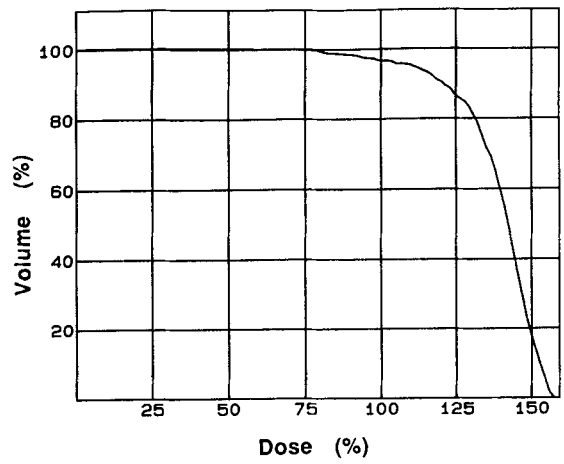
The resulting dose distribution with the proposed technique is illustrated for one of the patients. This patient was planned and treated for a liver metastasis from a colonic adenocarcinoma. The diameter of the lesion was 6–7 cm. The dose planning was made with an intentionally heterogeneous target dose. In Fig. 7a the dose distribution is seen in one slice through the central part of the metastasis. The dose–volume histogram of the target is presented in Fig. 7b and that of the liver in Fig. 7c. The volume of the metastasis was 179 cm^3 and the volume of the liver was 1478 cm^3. Thus the volume of the metastasis was 12% of the liver volume. This patient was treated with two fractions with a two-month interval. The dose/fraction was 20 Gy in the periphery of the target, corresponding to

Table

Transversal plane								
Deviation (mm)	1	2	3	4	5	6	7	
Percent of examinations	0	14	47	18	14	0	7	
Longitudinal direction								
Deviation (mm)	3	4	5	6	7	8	9	10
Percent of examinations	8	8	69	0	0	4	0	12



a)



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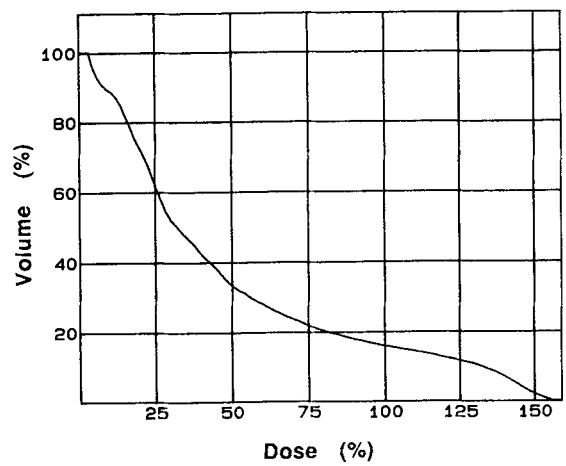

c)

Fig. 7. a) Relative dose distribution at the central part of the metastasis. An eight beam technique was used. The isodose levels are 120%, 100%, 50%, 25% and 10%. b) Dose-volume histogram for the metastasis. c) Dose-volume histogram for the liver.

100% in Fig. 7. The maximum dose/fraction in the target was 31 Gy, and 50% of the target volume was given a dose/fraction of 28 Gy or more (Fig. 7b). From Fig. 7c it can be seen that 50% of the liver volume received a dose/fraction of less than 6.6 Gy and 25% of the liver volume received a dose/fraction of less than 3.8 Gy. The maximum dose/fraction in the intestine was about 5 Gy. The total time for set-up and irradiation of the eight beams was 45 min.

Discussion

From the Table it can be concluded that in 93% of the examinations the deviation in the transversal plane was within 5 mm, and in 100% within 7 mm. In the longitudinal direction 88% of the examinations had a deviation within 8 mm, and in no case larger than 10 mm. It can thus be concluded with a margin of 5 mm to the tumor in the transversal plane and 8 mm in the longitudinal direction the minimum target dose will at least be equal to the specified periphery dose in about 90% of the treatments. However, even with smaller margins a high minimum dose will be obtained in tumors located in the liver or lung. The reproducibility of the skeleton was significantly better, than that described above for tumors in liver and lung. High reproducibility can thus be expected for retroperitoneal tumors.

Studies on the tolerance to partial liver irradiation suggest a large volume dependence of the dose–response function (2). These authors (2) have determined parameters in a normal tissue complication probability (NTCP) biological model for development of radiation hepatitis at 1.5 Gy per fraction. The values derived by the NTCP model have been used in the present study and dose-response curves have been calculated for the whole liver, half of the liver and a quarter of the liver. The values used were $TD_{50} = 45$ Gy, $m = 0.15$ and $n = 0.69$. The results shown in Fig. 8 suggest

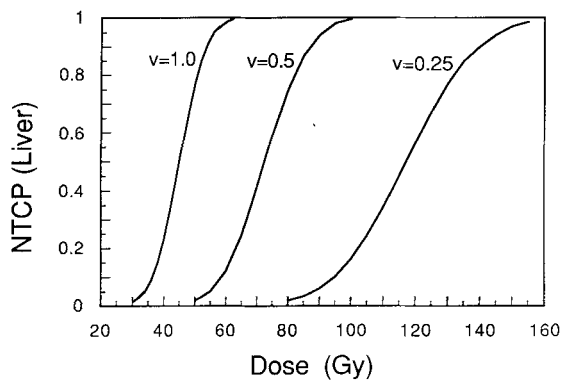

Fig. 8. Dose–response curves for radiation hepatitis for the whole liver (v = 1.0), half of the liver and a quarter of the liver volume. The curves were calculated with the NTCP model with data from Lawrence et al. (2).

that the dose can be increased considerably using partial liver irradiation before radiation hepatitis will appear. Experimental data from partial liver irradiation in animals also suggest a high tolerance (7).

A single-dose of 20 Gy will be equivalent to a dose, with 2 Gy/fraction, of about 50 Gy for an early responding tissue ($\alpha/\beta = 10$) (8), which is also thought to be representative for most tumors (9). For the normal liver with $\alpha/\beta = 2.5$ (2) a single dose of 20 Gy will be equivalent to a dose of about 100 Gy with 2 Gy/fraction (8). This high dose in the normal liver will be obtained only to a relatively small volume close outside the tumor due to the rapid decrease in dose outside the target (cf Figs. 6 and 7). An improved therapeutic ratio is theoretically obtained by increasing the number of fractions with a lower dose per fraction. However, the present treatment method, with a few high-dose fractions, is primarily based on three practical and theoretical considerations: 1) Few fractions makes it possible in clinical practice to put larger efforts in every treatment to assure a high geometrical accuracy in the dose delivery and thus reduce the set-up margin; 2) The volume dependence of the dose–response function of the liver may justify the theoretically decreased therapeutic ratio with a few fractions, still keeping the risk of long-term complications at an acceptable level; 3) The resource allocation at the radiotherapy department will be acceptable for a few fractions using the present 6–8 beam non-coplanar technique.

A heterogeneous dose in the target, with a high central dose, has been used in interstitial radiotherapy throughout the history of brachytherapy. In external beam radiotherapy, the conventional method to give a boost dose is the shrinking field technique or the simultaneous boost technique (10, 11). In the present paper an external beam radiotherapy boost method is used that was described in detail by Lax (4) for use in radiosurgery. A heterogeneous dose distribution with a high maximum dose in the centre is obtained with a marginal increase in dose outside the target (cf Figs 6 and 7). A prerequisite for this method is that many beams are used which are spread within a large solid angle (4). The method is thus not applicable to conventional radiotherapy techniques with very few beams. The proposed method can be expected to give favourable results for tumors in large organs with a high tolerance to partial volume irradiation. Thus, liver and lung are organs that could be expected to be suitable for treatment of relatively large targets with this method.

Stereotactic radiosurgery of brain metastasis has proven to be a successful palliative treatment method. The present stereotactic radiotherapy method may also be expected to have a clinical value in palliative treatments of extracranial targets. However, combined with conventional fractionated radiotherapy for volumes with microscopic involvement the method may have a value also for treatments with a curative intent.

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