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IRRADIATION OF SMALL STRUCTURES THROUGH THE INTACT SKULL

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Narrow beams of penetrating ionizing radiation may be used to transfer radiation energy to affect small, well circumscribed tissue volumes in the depth of the brain for functional neurosurgery and for treatment of small benign tumours. This kind of 'neurosurgical' operations through the intact skull is considered to give essential advantages over existing so-called 'open' methods (LEKSELL 1951, 1966). The physical conditions for the use of ionizing radiation for these purposes are today relatively wellknown, mainly through the work with the cyclotrons at Berkeley and at Uppsala (LARSSON 1962, LAWRENCE et coll. 1962, TOBIAS et coll. 1964, LARSSON & SARBY 1975) but, unfortunately, there exists no suitable construction that permits routine use in the hospital. The technical and physical aspects of this problem have therefore been considered and a ^{60}Co apparatus proposed. The work was done in close collaboration with the neurosurgeon (LEKSELL 1971).

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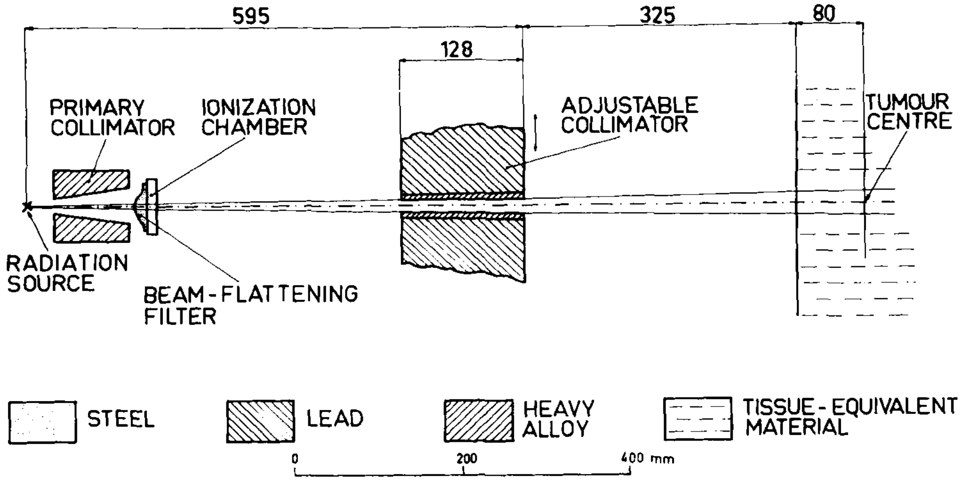


Fig. 1. Experimental lay-out for determining with photographic dosimetry, in a tissue equivalent phantom, the distribution of absorbed dose at irradiations with 6 MV roentgen beams shaped to define geometrical cross sections of 10 mm × 10 mm and 30 mm × 30 mm.

The term radiation surgery is here taken to represent various procedures employing localized irradiation for the destruction of small, mostly deep-lying, regions of tissue, healthy or neoplastic, for therapeutic purposes. Such techniques should be considered supplementary to various physical methods of open surgery employing local application of heat, cold, radiation from interstitial sources or ultrasound. A first attempt to use external irradiation for functional surgery was made by LEKSELL et coll. (1955) who reported on the use of conventional roentgen radiation and a stereotaxic instrument for tractotomy in cases of psychic disorder. It was soon realized, however, that more penetrating and geometrically well-defined radiation had to be used to permit the precise administration of necrotizing doses of radiation to circumscribed tissue volumes without untoward injury to surrounding structures. LIDÉN (1957) thus presented a preliminary analysis of the physical possibilities and recommended the use of 10 to 20 MV roentgen radiation or high-energy ion beams.

The following requirements on the technique should be met:

1) The apparatus should be so constructed that irradiation could be performed with sufficiently good precision in the administration of the desired dose to the localized target volume in the brain. As a basis for establishing the physical requirements of the technique the conditions for similar operations

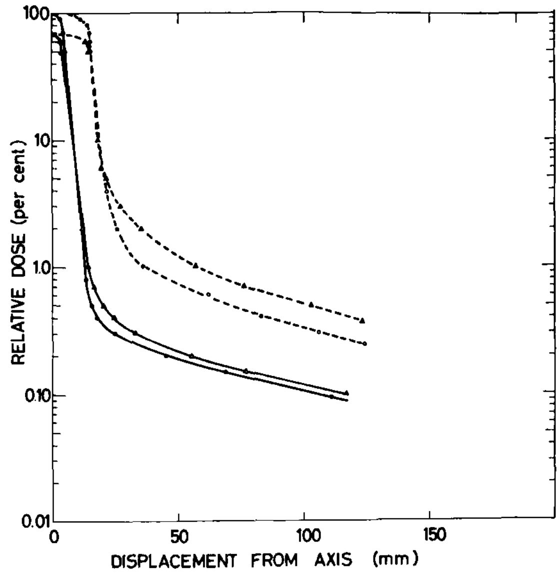


Fig. 2. Distribution of absorbed dose in a transverse plane at phantom depths of 1.5 cm (●—●—●, ○—○—○) and 8 cm (△—△, ▲—▲) for 10 mm and 30 mm wide 6 MV roentgen beams, respectively. The curves are normalized relative to the dose on the beam axis at a depth of 1.5 cm. The dose gradient in the penumbra regions of the beams is similar to that obtained for 2.5 mm proton and gamma beams (Fig. 4).

with the 185 MeV proton synchrocyclotron at Uppsala were accepted (LARSSON et coll. 1963).

2) Clinical demands for acceptable treatment times and free space for the patient around the isocentre should be fulfilled.

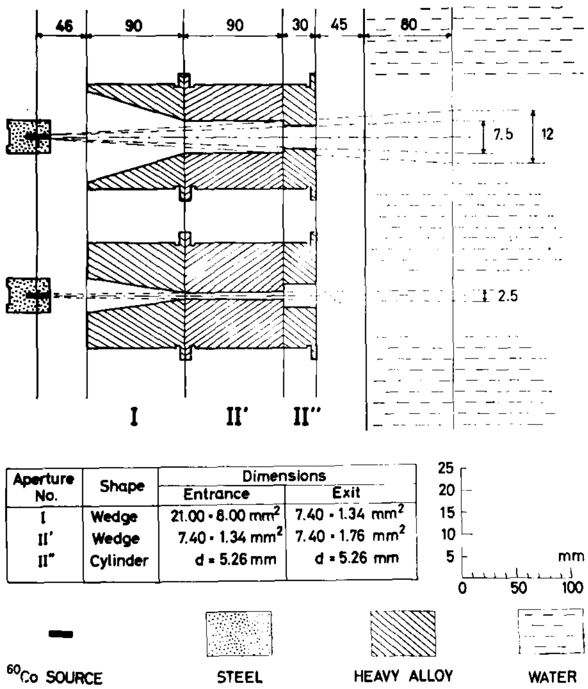
3) The radiation energy absorbed in the whole brain, that is the 'integral dose', should not be greater than that usually accepted as a tolerable single integral dose in radiation therapy of malignant brain tumours.

4) Current recommendations for radiation protection of the body of the patient and for the personnel should be fulfilled (ICRP 1970). This also includes arrangements needed to guarantee proper function of the apparatus at start and stop as well as continuous supervision of the patient.

To these criteria should be added a great many practical aspects on the construction of the apparatus, particularly in regard to the desired adaptation of available stereotaxic localization techniques (LEKSELL 1971).

Methods

Dose distribution determinations under simulated conditions were performed in narrow beams of 185 MeV protons, ^{60}Co gamma rays and 6 MV roentgen radiation (Figs 1, 3). The centre of the target volume was assumed to lie at a depth of 8 cm in a tissue-equivalent phantom, the mean radius of a normal



Aperture No.	Shape	Dimensions Entrance	Exit
I	Wedge	21.00 · 8.00 mm²	7.40 · 1.34 mm²
II'	Wedge	7.40 · 1.34 mm²	7.40 · 1.76 mm²
II"	Cylinder	d = 5.26 mm	d = 5.26 mm

Fig. 3. Experimental lay-out for determining with photographic dosimetry, in a tissue-equivalent phantom, the distribution of absorbed dose at irradiation with a ^{60}Co beam shaped to define a geometrical cross section of 2.5 mm × 7.5 mm.

skull. The methods used were described in detail by LARSSON & SARBY (1975) and SARBY 1974.

The geometrical demands on the single ^{60}Co gamma beam channel was discussed by SARBY (1974). In order to optimize the collimation of a narrow gamma beam a collimating arrangement was constructed in 17.2 g/cm³ heavy alloy (Fig. 3). It consisted of one primary collimator (I) and two beam-defining collimators (II' and II") and it was mounted in an irradiation geometry similar to that of the discussed treatment apparatus.

The roentgen beams were produced with a 6 MeV linear accelerator for radiation therapy (Varian V-7705 Clinac; AUSTIN 1964). The irradiation geometry appears in Fig. 1. The accelerator produced radiation with a mean dose rate of about 200 rad/min in pulses with a duration of 1 μs and a separation of 5 ms. The diameter of the focus was approximately 3 mm.

Calculation of superposed dose distributions as a result of irradiation with multiple beams was made with computer programs described by DAHLIN (1970) and DAHLIN & SARBY (1975) (Fig. 7). The spatial distribution of the beams was defined by means of a coordinate system (Fig. 6).

Measurements at the ^{60}Co apparatus. The dose rate at the beam focus of the ^{60}Co unit was determined from measurements at the centre of a spherical plexiglass phantom (diameter 16 cm) with LiF plates (1 mm × 4 mm × 4 mm). The dosemeters were calibrated in a water phantom irradiated with a broad ^{60}Co gamma beam. The doses were calculated according to a formula derived by BURLIN (1966) with an overall uncertainty of ± 5 per cent.

Secondary radiation doses to various structures in the head and to different organs in the body were measured with LiF teflon rods (diameter 1 mm, height 4 mm) in a tissue-equivalent whole body phantom and on patients irradiated by the ^{60}Co unit. The dosemeters were calibrated in a broad ^{60}Co beam and their energy dependence for the degraded photon energy in different parts of the body was not of significance for the results.

Results and Discussion

Radiation

The radiation should have sufficient penetrability and little scattering in the passage through the tissues of the head to selectively destroy tissue volumes of diameters about 2 to 12 mm at depths of 6 to 10 cm. The demands on the distribution of absorbed dose in the brain can be specified from the experiences of earlier attempts to produce useful radiation lesions in experimental animals or patients (LARSSON et coll. 1963) and from the irradiation of brain tumours (LINDGREN 1963): (1) The absorbed dose in the target volume should be about 20 krad in one single irradiation; (2) The distribution of absorbed dose should have a large gradient in the border zone of the desired lesion; (3) Immediately outside the planned lesion the absorbed dose must be as low as possible and not exceed 5 krad; (4) The average dose in the brain should be as low as the conditions permit and should not be considerably higher than approximately 100 rad.

The technical situation today in regard to radiation sources and radiation handling is of primary concern. Omitting, for practical and economical reasons, the previously used light ions, i.e. high-energy protons, deuterons or alpha particles, there are four kinds of more easily available ionizing radiation the penetration of which should permit irradiation of target volumes near the centre of the head: high-energy electrons, supervoltage radiation, gamma radiation from nuclides and fast neutrons. All these radiations are, in principle, useful for the purpose. However, the choice between them requests detailed consideration of their attenuation, absorption and scattering properties with the view towards the possibility of obtaining well-defined narrow beams during the passage through the tissues.

Table 1

Possible gamma emitting nuclides for cerebral radiation surgery

Nuclide	Half-life $T_{\frac{1}{2}}$ (day)	Photon energy* (abundance per disintegration) (MeV)	Mean energy E_a (MeV)	Photons per disintegration
^{46}Sc	84	0.89 (1.00); 1.12 (1.00)	1.00	2.0
^{60}Co	1 920	1.17 (1.00); 1.33 (1.00)	1.25	2.0
^{160}Tb	73	1.27 (0.07); 1.18 (0.15); 0.97 (0.31); 0.88 (0.31); 0.30 (0.30)	0.81	1.14
^{182}Ta	115	0.22 (0.08); 1.12 (0.34); 1.16 (0.03); 1.19 (0.16); 1.22 (0.45)	1.11	1.06
^{192}Ir	74	0.885 (0.005); 0.612 (0.06); 0.604 (0.09); 0.589 (0.04); 0.468 (0.49); 0.317 (0.81); 0.308 (0.30); 0.296 (0.29)	0.37	2.1

* Only important components are given

High-energy electrons are similar to the protons previously used to some success for radiation surgery since they are uni-charged atomic particles travelling with a velocity approaching that of light. On their way through the tissues they interact almost continuously with the molecular electronic structure and thus energy is transferred to the tissue along near-rectilinear tracks. Only the high-energy part of the electron track is of interest. The considerable spread of the beam through successive scattering of the particles make impossible the use of the last, say, 10 cm of the range for selective irradiation of small tissue volumes. Demanding that the radiation has to pass intervening tissues of not less than 8 cm thickness this condition means that we have to choose a range of at least approximately 20 cm which corresponds to a kinetic energy of 40 MeV. At this energy the electron has a mass 80 times larger than the mass at rest, a fact that explains why such particles can move nearly rectilinearly through tissue. Nevertheless, they are much more influenced by elastic multiple scattering against atomic nuclei than 185 MeV protons, which are, under the conditions considered, another factor of 25 heavier. The importance of these differences in regard to scattering is considerable. Besides of reducing the gradient of the dose distribution at the geometrical edges of the beam, the phenomenon contributes to the strongly falling central depth dose distribution in an electron beam of otherwise suitable range. The shape of this curve is not known for relevant beam diameters but the depth dose curve of electrons (BRAHME 1971) would probably be significantly inferior to the corresponding curves for 185 MeV protons (LARSSON & SARBY) or ^{60}Co gamma radiation (SARBY). The fact that electrons in the energy range 30 to 40 MeV can be produced with commercially available small accelerators at reasonable cost means that they may become of practical interest for radiation surgery. However, electrons seem to offer no advantages over, for example, gamma radiation from ^{60}Co or supervoltage roentgen radiation. The latter type of radiation can also be produced by electron accelerators, at lower energy and cost.

Supervoltage roentgen radiation. At sufficiently high energy, roentgen radiation can be used for precise irradiation of tissues at the depth. Characteristic for such radiation is that the photons are distributed over a continuous energy spectrum in which the single photon can have an energy varying from that of the accelerated electrons down to a relatively low threshold. The shape of the spectrum is also dependent on target material and filtration (BRYNJOLFSSON & MARTIN 1971, JESSEN 1973). In the actual energy range, the mean energy of the photons is about one third of the electron energy. These circumstances mean, for example, that ^{60}Co gamma radiation, with an average energy of 1.25 MeV, is approximatively equivalent to roentgen radiation produced at an acceleration potential of 4 MV. Correspondingly, gamma radiation from ^{192}Ir, at an average energy of 0.37 MeV, may be said to correspond to 1 MV roentgen radiation.

From the principal point of view, therefore, it is not necessary to differentiate between roentgen and gamma radiation. Difficulties are more of a practical nature when the choice is to be made between roentgen radiation from electron accelerators and gamma radiation from nuclides. On one side the roentgen radiation from commercial linear accelerators for radiation therapy in the range 4 to 15 MeV permits high dose rates and well-collimated beams and they also give better flexibility because arbitrary directions of the beam relative to the head of the patient can be chosen in comparison with a ^{60}Co equipment that necessarily has to employ a multiple beam arrangement (vide infra). However, presently employed systems of acceleration and beam transport do not permit the desirable precision in the position and size of the focus and without further improvement they are not suitable for the purpose discussed. Further, the mechanical precision has to be improved to permit desired alignment of beam axis with the isocentre. Today the position of the isocentre of commercial apparatus is normally located within a sphere of 1 mm radius.

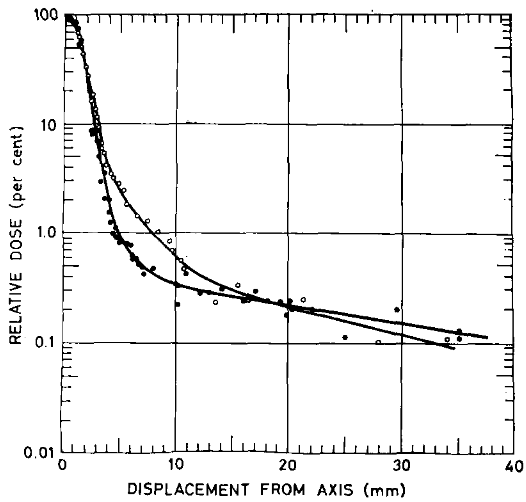


Fig. 4. Distribution of absorbed dose in a transverse plane at a depth of 8 cm in tissue irradiated by a 2.5 mm wide ^{60}Co beam (●) under the conditions shown in Fig. 3. For comparison the corresponding distribution for a 185 MeV proton beam (○) is given.

Indeed, the experimental results revealed the usefulness of ^{60}Co gamma radiation (Figs 4, 5 and SARBY 1974). Approximately, the conclusions arrived at should be valid also for roentgen radiation from comparable electron accelerators. This is evident from the measurements on 10 mm and 30 mm wide roentgen beams (Fig. 2). The results (Fig. 2) showed almost the same dose gradients in the penumbra region of the beams as those obtained for narrow 185 MeV proton beams and ^{60}Co gamma ray beams (Fig. 4). The dose levels outside this region were also almost the same. At higher energies of the roentgen radiation the diffusion of long-range secondary electrons may seriously widen the penumbra region of the beams. At higher energies the higher cost further becomes a significant disadvantage for this type of apparatus.

The choice between the two alternatives, i.e. roentgen or gamma radiation, should be based on technical, clinical and economical rather than physical considerations. If radiation surgery will reach a position as a standard procedure, improved electron accelerators for roentgen production, adapted for the purpose, would seem a most attractive alternative.

Nuclides. Gamma-emitting nuclides have some advantages in the present context. Once installed, they are easy to handle and, most important, they permit unique reproducibility of the physical conditions during treatment. The proposed apparatus for cerebral radiation surgery with a great number of individually radiating gamma sources was based on the data for the gamma-emitting nuclides presented in Table 1. With the availability of high flux density nuclear reactors giving 10^{13} to 10^{14} neutrons/cm$^2\cdot$s, it has been possible

Table 2

Data used for calculation of the activity per cm³ for the various nuclides

Mother nuclide (atomic mass A-1)	Weight fraction in the natural abundance of the element h	Density ϱ ($g \cdot cm^{-3}$)	Cross-section for production of the daughter nuclides in Table 1 σ (barn)	Maximum activity per cm³ of the daughter nuclide $a_{(max)}$ ($Ci \cdot cm^{-3}$)
^{45}Sc	1.00	2.9	23	2 400
^{59}Co	1.00	8.9	37	9 100
^{159}Tb	1.00	8.2	46	3 900
^{181}Ta	1.00	16.6	21	3 100
^{191}Ir	0.385	22.4	1 000	74 000

Table 3

Product of the build-up factor and decay factor ($f_b \cdot f_d$) for various periods of activation (τ) and cooling (t) expressed in half-lives ($T_{\frac{1}{2}}$)

$\frac{\tau}{T_{\frac{1}{2}}}$ \ $\frac{t}{T_{\frac{1}{2}}}$	0	0.25	0.50	1.0	2.0	3.0
0.25	0.159	0.134	0.112	0.080	0.040	0.020
0.5	0.293	0.246	0.207	0.147	0.073	0.037
1.0	0.500	0.421	0.353	0.250	0.125	0.063
2.0	0.750	0.631	0.530	0.373	0.188	0.094

to produce sources of various gamma-emitting nuclides of high specific activity, suitable for radiation therapy. It soon became clear that ^{60}Co was the only nuclide that today completely fulfils the demands. Its relatively long half-life, 5.3 years, suitable gamma energies, and relatively high production cross section are all convenient. Other possible nuclides considered have less suitable half-lives and cannot be easily produced in required amounts (Tables 1 to 6). The mechanical and chemical properties of the target material must also be taken into account.

Table 4

Activity per cm³ for the various nuclides at optimum conditions for activation and decay

Nuclide	Period of activation and decay $\tau = t$ (days ca.)	Activity per cm³, a_V according to equation 2 ($Ci \cdot cm^{-3}$)			
		$\eta \cdot \varphi = 1$*	$\eta \cdot \varphi = 0.5$*	$\eta \cdot \varphi = 0.2$*	$\eta \cdot \varphi = 0.1$*
^{46}Sc	170	450	230	90	45
^{60}Co	1 000	1 800	900	360	180
^{160}Tb	150	730	370	150	73
^{182}Ta	230	580	290	120	58
^{192}Ir	150	14 000	7 000	2 800	1 400

* in 10^{14} neutrons per cm² and s

Table 5

The length of the sources and the total activity of the apparatus, calculated for 180 sources, cross section 0.008 cm², $f_b \cdot f_d = 0.2$ after activation with 0.5×10^{14} neutrons per cm² and s

Nuclide	Linear attenuation coefficient for the source material* (cm^{-1})	Length of the sources L (cm)	Total volume of the sources (cm³)	Total activity in the apparatus	
				Nominal activity A_t (Ci)	Equivalent activity A_e (Ci)
^{46}Sc	0.173	5.3	7.2	1 700	2 200
^{60}Co	0.47	2.0	2.9	2 500	3 300
^{160}Tb	0.59	1.6	2.3	850	630
^{182}Ta	0.99	0.93	1.3	380	260
^{192}Ir	5.1	0.17	0.25	1 800	2 400

* Corresponding to the mean energy E_a of the photons

All the nuclides considered in Table 1 are produced by neutron capture reactions, the activity per cm³, a_v, produced (in Ci/cm³) after τ months of irradiation and t months of cooling being

$$a_V = 1630 \cdot \frac{\varrho \cdot h \cdot \sigma \cdot \varphi \cdot s \cdot \eta}{A-1} \cdot \left(1 - e^{-0.693 \cdot \frac{\tau}{T_{\frac{1}{2}}}}\right) \cdot e^{-0.693 \cdot \frac{t}{T_{\frac{1}{2}}}} \tag{1}$$

where ϱ is the density (in g cm^{-3}), h the concentration in the target (weight

Table 6

Dose rates at a depth of 8 cm in tissue at beam focus of an apparatus of the same geometry as the suggested ^{60}Co unit, calculated for sources according to Table 5

Nuclide	Equivalent activity A_e (Ci)	Mean energy of the photons E_a (MeV)	Linear attenuation coefficient for tissue μ (cm^{-1})	Linear energy absorption coefficient for tissue μ_{en} (cm^{-1})	Dose rate $\dot{D}$ ($rad \cdot h^{-1}$)
^{46}Sc	2 200	1.00	0.071	0.031	4 400
^{60}Co	3 300	1.25	0.063	0.030	8 700
^{160}Tb	630	0.81	0.078	0.032	1 000
^{182}Ta	260	1.11	0.067	0.030	590
^{192}Ir	2 400	0.37	0.11	0.033	1 400

fraction) and σ the cross section of the mother nuclide of atomic mass A—1 for neutron capture (in 10^{-24} cm^2) (LEDERER et coll. 1967). The factor s (always close to 1) corrects for the decrease in concentration due to consumption of the mother nuclide in the process. Similarly, the factor η reflects the decreased efficiency of activation due to the fact that the efficient flux density in the target may be very different from the nominal flux density φ (in 10^{14} neutrons/cm$^2 \cdot$s) due to attenuation in target and capsule materials. Table 2 gives, besides the physical characteristics of the target material, the maximum activity per cm^3, a_{max}, which would be achieved at equilibrium after irradiation of 10^{14} neutrons/cm$^2\cdot$s provided s = 1 and η = 1. For convenience, the build-up factor $f_b = \left(1-e^{-0.693\frac{\tau}{T_{\frac{1}{2}}}}\right)$ and the decay factor $f_d = e^{-0.693\frac{t}{T_{\frac{1}{2}}}}$ are given separately in Table 3. The activity per cm^3 achievable during varying conditions of activation can now be calculated from the formula

$$a_v = a_{max} \cdot \eta \cdot s \cdot \varphi \cdot f_b \cdot f_d \qquad (2)$$

which includes two factors f_b and f_d for build-up and decay, respectively.

With a view towards ^{60}Co typical periods of activation are assumed to be $\tau = t = 0.5$ half-lives, giving $f_b \cdot f_d = 0.2$, s to be 1.00 and η to vary between 0.1 and 1. The result, for a nominal neutron flux density of 10^{14} cm^{-2} s^{-1} ($\varphi = 1$) is presented in Table 4, together with similarly typical data for the previously considered nuclides.

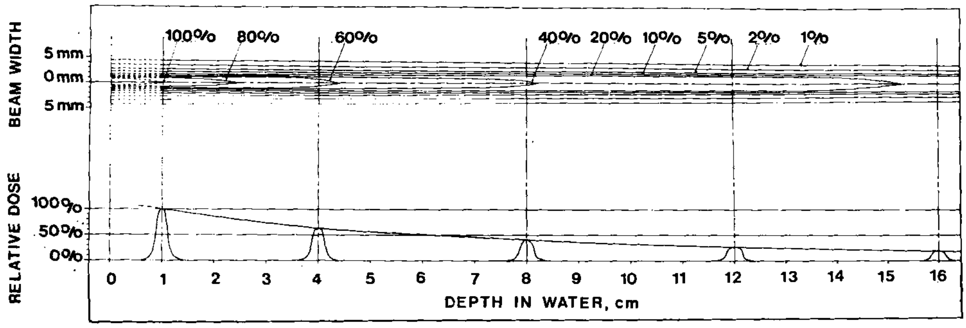


Fig. 5. Isodose curves for a 2.5 mm wide ^{60}Co beam measured in a coaxial plane, (the upper part of Fig. 3) and normalized to 100 % at a depth of 1 cm.

To arrive at an estimate of practically achievable dose rates we further assume the multiple-beam device to contain 180 cylindrical sources (length L cm, cross section 0.008 cm^2) and that irradiation takes place under the condition $f_b \cdot f_d = 0.2$ and $\eta \cdot \varphi = 0.5 \times 10^{14}$ $cm^{-2}\,s^{-1}$. The length of the sources (Table 5) was considered to be optimal when the utilization factor due to the influence of self-absorption in the source was 65 per cent (SARBY 1974). Under these conditions the total activity A_t in the apparatus will be, for ^{60}Co, 2500 Ci (for comparison with other nuclides see Table 5). It is convenient to calculate the activity A_e of an equivalent point source, producing one gamma photon per disintegration. With the source-centre distance, 38 cm of the suggested apparatus (Figs 3, 8), and representing the head by a concentric tissue-equivalent sphere of 8 cm radius, the dose rate $\dot{D}$ (rad h^{-1}) at the centre assuming narrow beam attenuation will be (SARBY 1974):

$$\dot{D} = 117 \cdot A_e \cdot E_a \cdot \mu_{en} \cdot e^{-\mu \cdot 8} \qquad (3)$$

where E_a (MeV) is the mean gamma energy per disintegration (Table 1) and μ_{en} and μ, respectively, the linear energy absorption coefficient and linear attenuation coefficient for water in cm^{-1} (Table 6). The result for ^{60}Co, 8700 rad h^{-1}, is given in Table 6 together with data of the other nuclides considered.

Cobalt-60 is thus presently to be considered the obvious choice although some of the other nuclides are potentially interesting. Particularly ^{192}Ir with, theoretically, very high maximum activity per cm^3 and convenient mechanical and chemical properties is recommended for further testing especially when higher neutron flux densities will be available. The disadvantageous short half-life may be compensated for by designing convenient source exchange.

Table 7

Data for dose calculations on narrow neutron beams

Neutron energy E (MeV)	Free mean path λ (cm)	Linear attenuation coefficient μ (cm^{-1})	Coefficient for imparted energy a_E (erg cm^2 g^{-1})	Relative dose at a depth of 8 cm in tissue	Fluence rate for attaining 10 krad per hour at a depth of 8 cm (cm^{-2} s^{-1})
1.0	2.5	0.40	0.29×10^{-6}	0.04	24×10^9
2.0	4	0.25	0.35×10^{-6}	0.14	5.7×10^9
5.0	7	0.14	0.55×10^{-6}	0.33	1.5×10^9
10	9	0.11	0.63×10^{-6}	0.41	1.1×10^9
15	10	0.10	0.71×10^{-6}	0.45	0.9×10^9

The energy of the radiation is low, but still high enough to ascertain the demands above of the dose distribution at the centre of the brain. Further, it would allow convenient radiation shielding. ^{46}Sc might also be a possible future alternative.

Fast neutrons, here considered for the energy range 1 to 15 MeV, interact with tissue predominantly by elastic collisions with hydrogen. They have a free mean path λ (2.5 to 10 cm) roughly varying linearly with the energy. In total, the absorption is very complex but approximately the dose distribution along the axis of a narrow neutron beam can, as for the gamma beams (SARBY) be attributed to the first collision, an approximation valid because of the short range of the recoil particles.

The dose rate, $\dot{D}(z)$ $erg \cdot g^{-1} \cdot s^{-1}$ (well approximated by the kerma rate) at a depth of z (cm) in tissue irradiated with a beam containing monoenergetic (E MeV) neutrons of a flux density φ (z) ($cm^{-2} \cdot s^{-1}$) is given by:

$$\dot{D}(z) = a_E \cdot \varphi(z) = a_E \cdot \varphi(o) \cdot e^{-\mu z} \tag{4}$$

where the attenuation coefficient $\mu = \frac{1}{\lambda}$ (cm^{-1}) and a_E is an energy transfer coefficient ($erg \cdot cm^2 \cdot g^{-1}$) given by the expression:

$$a_E = \sum_k \sum_l N_k \cdot \sigma_{k_l}(E) \cdot t_{k_l} \text{ (E)} \tag{5}$$

with N_k the number of atom species K per cm^3, σ_{k_l} (E) the cross section for any interaction (l) involving element K, and t_{k_l} (E) the total energy imparted to secondary radiations as a result of this interaction (ROSSI 1956). Relevant

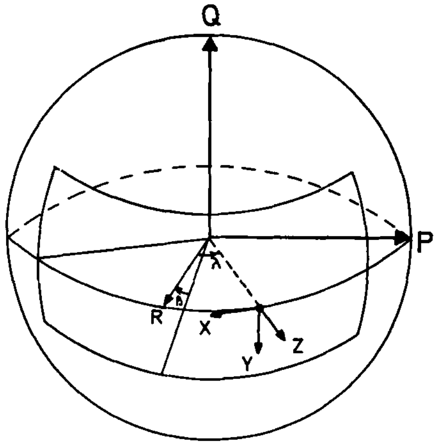


Fig. 6. The spherical coordinate system P, Q, R for the definition of the beam channels in space.

data for calculation from equations (4) and (5) the absorbed dose in soft tissue having the chemical net formula $(C_5H_{40}O_8N)_n$ and 1 g cm^{-3} density are given in Table 7.

The relative biologic efficiency for fast neutrons is between 2 and 5, implying that a dose of 4 to 10 krad would be needed for necrotizing a small tissue volume with neutrons. Flux densities of the order of 10^9 cm^{-2} s^{-1} or more are required to deliver the necessary dose in approximately one hour (Table 7). However, existing neutron sources cannot produce well collimated beams with such high fluence rates at present. Thus, utilization of a nuclear reactor is technically not realistic, neither is the use of neutrons produced by nuclear reactions induced by alpha emitting nuclides suitable. A ^{210}Po-beryllium source, ($T_{\frac{1}{2}}$ = 138 days), giving neutrons of a mean energy of about 5 MeV, would have to represent an activity of the order of 1 MCi to reach the same dose rate as for the ^{60}Co apparatus in question; ^{252}Cf ($T_{\frac{1}{2}}$ = 1.6 y) emits 2.3×10^6 neutrons/μg · s with a mean energy of 2.3 MeV and also 1.3×10^7 photons. At present, the cost of a ^{252}Cf source of sufficiently high activity would be tremendous. Today, the most favourable neutron source, physically and technically, seems to be the 'D-T generator'. It produces 14 MeV neutrons from a tritium target bombarded with low-energy deuterons. However, the dose rate would be unsatisfactory low even for radiation therapy, approximately 10 rad/min. Thus, it can be concluded that fast neutrons present no alternative to electro-magnetic radiation in clinical radiation surgery.

Relative biologic efficiency

The possibilities of attaining a similar biologic effect with narrow beam techniques based on different types of radiation are dependent both on the

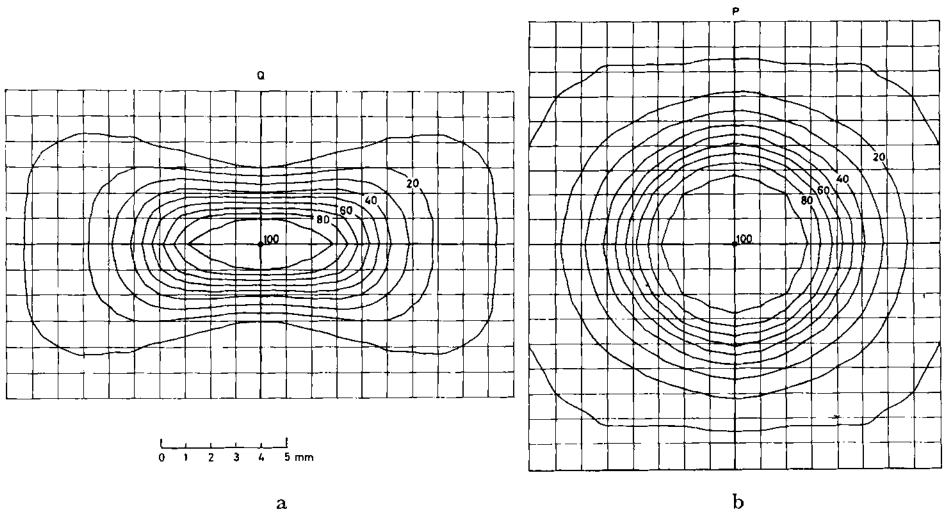


Fig. 7. Calculated distribution of dose as a result of superposed irradiation by 179 beams with a geometrical cross section of 3 mm × 7 mm all directed towards a common centre of irradiation (the beam focus). The brain is simulated of an isocentric spherical water phantom, 16 cm in diameter. The calculations refer to twoperpendicular planes a) P = 0 and b) Q = 0 with the beams distributed within $\beta = \pm 35°$ and $\lambda = \pm 80°$ according to the coordinate system defined in Fig. 6. The beam geometry is identical with that chosen in the actual construction (Figs 8, 9). Related to the patient the dose distributions refer to (a) sagittal plane and (b) frontal plane.

macroscopic dose distribution and on the microscopic energy absorption in time and space. The biologic efficiency of untested types of radiation can be predicted from a comparison of LET distributions. Thus, the possibilities o using ^{60}Co radiation or supervoltage roentgen radiation can be considered on the basis of the conditions for 185 MeV proton radiation as a reference (LARSSON 1962, LARSSON & SARBY 1975). All three types of radiation can be characterized as 'low-LET' radiation and have similar LET distributions (ICRU 1970). This means that after the passage of a primary ionizing particle in a cell the initial spurs with diameters up to 2 nm are well isolated, with a mean separation of 100 nm. It is therefore improbable that interaction between diffusing reaction products from one spur to another will influence the biologic efficiency of these radiations.

The probability of reactions between spurs from two different primary particles passing through a cell depends on the momentary fluence rate in the beam, which is to be considered relative to the convenient mean dose rate (100 to 1000 rad/min) for the clinical applications. If this probability is to be

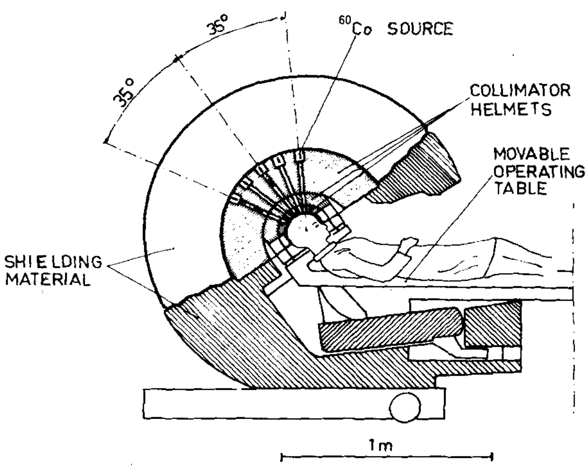


Fig. 8. Section through the apparatus with ^{60}Co gamma radiation with patient in position for irradiation. Five of the beam channels are shown. The diagram refer to the plane P = 0 in Fig. 6. (The apparatus was manufactured by AB Motala Verkstad, Motala, Sweden.) The system of collimators (mounted in steel helmets) and steel shields is also indicated.

of the same size as the probability for the interspur reactions mentioned above, the mean distance between the primary particles also must be about 100 nm. The situation arises when the beam contains 10^{10} particles per cm^2 within a period shorter than the life time of the reaction products ($\leqslant 10^{-4}$s), which is a condition that cannot be met for a ^{60}Co technique.

Accelerators for light ions and roentgen radiation produce radiation in pulses 1 to 10 μs long with intervals of 1 to 100 ms, also implying that the mean dose rate mentioned corresponds to a fluence per pulse of much less than 10^{10} particles per cm^2. Consequently, regarding the time distribution of energy absorption for the discussed types of radiation, differences in their biologic efficiencies are unlikely. That these types of radiation have the same biologic efficiency when used for radiation therapy with broad beams has been concluded from a review of a large number of examinations (Sténson 1969).

Design of an apparatus for ^{60}Co gamma radiation

The criteria out-lined on p. 513 to 514 lead to the following demands on field size, distribution of dose and minimum dose rate in the target area: (1) The geometrical beam cross section should be from 3 mm × 5 mm to 3 mm × 12 mm; (2) a dose of approximately 20 krad should be given to the target centre within 3 hours or less; (3) the expected border zone (at the level of the highest dose gradient) between the area of necrosis and, practically, non-affected tissue should be as narrow as possible.

By accepting ^{60}Co gamma radiation the main lines of a possible construction emanate directly, as the dimensions of the radiation shield and the available

Table 8

Secondary radiation doses to various parts of the body at a given dose of 20 000 rad to the centre of the target volume

Part of body	Absorbed dose (rad)
Blood-forming organs*	30
Gonads	6
Eye	24
Skull bone	24
Nasopharynx	38
Thyroid	42
Spinal cord	20 – 40
Lung	30
Kidney	6
Foot	2

* Estimated with respect to the distribution of red bone marrow in an adult person

pecific activity of ^{60}Co set practical limits for the distance between the radiation sources and the target centre. The material, some kilocurie of ^{60}Co, has to be divided into many thin needles permitting it to come close to the target without undue penumbra effects, a principle previously suggested for use in radiation therapy by Ellis & Oliver (1951). The distance between the sources and the beam focus, i.e. the point of intersection of the beam axes to which the centre of the target volume is to be positioned stereotaxically, is 38 cm (Fig. 8).

The single beam channel. Based on these considerations and detailed experiments of the system of beam collimation (Sarby) an attempt was made to optimize the collimation of a narrow gamma beam (Fig. 3) with the intention to reduce the possibilities for photons scattered in the walls of the primary collimator to reach the patient. Compared with the proton beam previously used for clinical applications the dose gradient in the penumbra region was somewhat more favourable for the gamma beam shaped with this system while the dose contributions outside the penumbra regions were about the same (Figs 4, 5).

However, because of high manufacturing cost for the collimator system (Fig. 3), the construction of the treatment apparatus had later to be based on a technical simplification, identical to the alternative C described by Sarby.

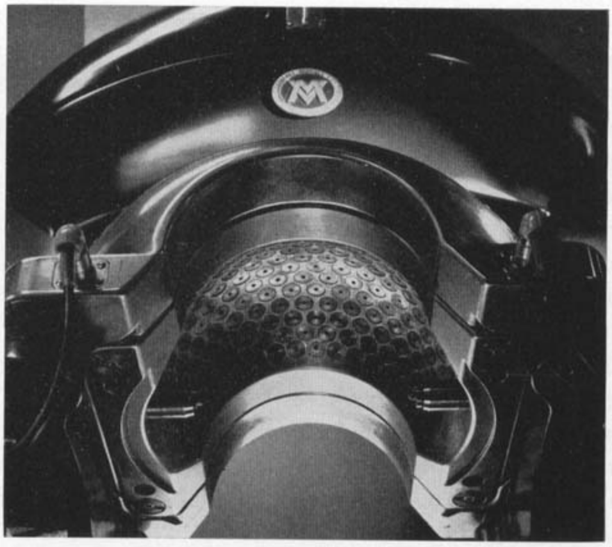


Fig. 9. The inner collimator helmet (Fig. 8), in position outside the apparatus, seen obliquely from underneath. The helmet is mounted at the operating table (Fig. 8). The horizontal spindles (coinciding with the P axis in Fig. 6) are used for fixation of the stereotaxic instrument.

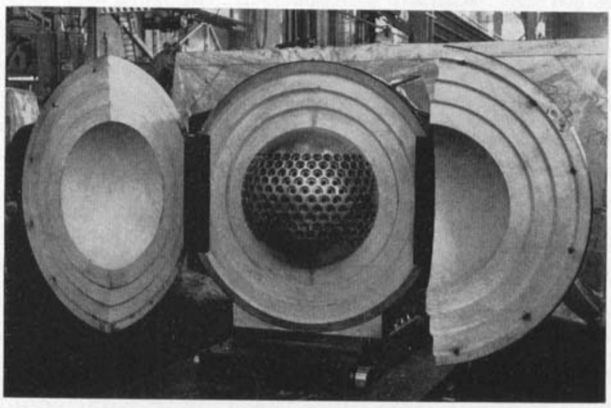


Fig. 10. Construction ready for loading with ^{60}Co. The system of concentric semi-spherical radiation shields is opened from the rear so as to show the position of holders for the source capsules.

It gave a slightly higher but still tolerable dose to the brain tissue outside the geometrical penumbra region of the beam.

The cross section of the individual beams was (as in Fig. 3) defined by sets of exchangeable collimators. For practical and economic reasons the collimators consisted of one set of permanent primary collimators and two sets of consecutive beam-defining collimators, mounted in spherical steel helmets, the inner being exchangeable so as to permit easy variation of the larger diameter of the cross section (Figs 8, 9).

The beam geometry. The number of beam channels is dependent on the total amount of ^{60}Co and its specific activity (Tables 4, 5). All sources are located on a spherical surface, the centre of which coincides with the beam focus (Fig. 8). The distribution of the sources of the sphere and the angles of incidence of the single beams determine, at given dimensions of the apparatus, the distribution of the absorbed dose in the brain. The positions of the sources may be defined by the latitude angle β and the longitude angle λ in a spherical coordinate system P, Q, R (Fig. 6). The equatorial plane $Q = 0$ and the polar axis both form 45° angle against the axis of the patient (Fig. 8). The sources are placed symmetrically in regard to the equator and they are almost uniformly distributed over the spherical sector $\lambda = \pm 80°$, $\beta = \pm 35°$.

The angle between two neighbouring sources varies between 8.1° and 10° and the corresponding distance is between 5.4 and 6.6 cm. This arrangement is dictated by the necessity to work with a large number of sources, presently 179 (the position $\lambda = 0$, $\beta = 0$ is used for accessory mechanical arrangements and a less precise burrhole is not used).

The distribution of the sources is as far as possible adapted to the demand for dose distributions suitable for disc-shaped lesions. The theoretically best solution is to distribute the sources as widely as possible within the meredian angular interval and at the same time, let the maximum latitude β_{max} be determined by the conditions of the gradient in the lesion's borderline. The choice of $\beta_{max} = 35°$ is aiming at a sufficiently steep dose in the border line of the lesion without adventuring its disc shape.

The resulting well-circumscribed, disc-shaped dose distribution (Fig. 7) was calculated for the case when all apertures were manufactured for a geometrical field size of 7 mm × 3 mm. An alternative dimension 5 mm × 3 mm was also tested clinically (LEKSELL 1971).

It must be clear that this construction with 179 different radiation sources is necessary only because the useful photon-yield per mm^2 effective source area is so low. In fact this yield is about 1000 times lower, than what could be obtained from a well focused electron beam from a linear accelerator. Thanks to the separation of the active material, however, the dose gradients may be kept large. Nevertheless irradiation could be performed in periods which are not more than a factor of 10 longer than those which would be used at an accelerator (Table 6).

The separation of the active material into many sources permits that the individual beam can be kept at the same position in relation to the object during the whole irradiation. The dose accumulated in the radiation field at the surface of the brain during a typical irradiation with 20 krad is then at most about 200 rad, that is a dose which locally applied should be well tolerated by all intervening tissues, if care is taken to avoid the eye lenses. Thus, it is evident that the need for rotation of the object during irradiation is eliminated. The result is in fact practically equivalent to one single beam passing over the whole spherical sector covered by the set of cobalt sources. The fine structure expected to occur by the many-field irradiation is not evident in or near the target area (Fig. 7). The parallel is strict also in regard to the relatively unimportant fact that the resulting rotation around two perpendicular axes is not constant but varies by the beam direction.

The unit was constructed with high mechanical precision in the collimating systems and in the alignment of the beam axes. The definition of the beam focus thus lay within a sphere with a radius of 0.1 mm.

Radiation protection. The external shielding consists of a spherical steel shell (Figs 8, 10) with a thickness of 35 cm as was concluded from Monte Carlo calculations performed by LEIMDÖRFER (1963). The fixture for the head of the patient firmly attached to a helmet containing the final collimator set moves with the stretcher in and out through an opening in the shell (Figs 8, 9); that the fixation is stable throughout the irradiation is indicated on the manoeuvre table. Visual and verbal contact with the patient can be kept during irradiation.

The penetration through the shielding, precalculated and checked by standard survey meters, was in conformity with current regulations for therapy equipments. Some secondary radiation emanated through the opening during irradiation; the risks for patients in reproductive age or pregnant patients may be estimated from Table 8. The radiation protection of the body is, even for patients in reproductive age, fully acceptable and seems to be comparable with that at other forms of radiation therapy in the head and neck region.

The integral dose to the brain for a central dose of 20 krad and a field of 5 mm $\times$ 3 mm was estimated to be about 150 kg rad.

Handling of the apparatus. The construction permits simplicity in handling which is exceptional compared to other radiation equipments. The patient is moved in and out of the apparatus by means of a pneumatic system.

A physicist must be responsible for the regular calibration of the dose rate, for the radiation safeness of patients and personnel, and together with the surgeon, for the treatment plan. With these precautions, however, the apparatus can be served by the ordinary staff of the clinic and it can be used, after determination of the individual depth dose factor for the mean depth of the target structure in the head, to administer accurate doses by means of a watch and a curve showing the dose rate as a function of the date of radiation.

Conclusions

The great advantage in the use of a nuclide in the present apparatus for cerebral radiation surgery is the absolute reproducibility which the procedure permits. Through the constancy of the decay of the nuclide, the radiation energy and the beam geometry, the dose distribution is fully reproducible from one patient to another. The only physical factor that varies slightly is the dose rate. Through strict control of this parameter, with knowledge of a possible dose rate dependence of the clinical effect, the operation can be given the character of a standard procedure, and that in the best physical meaning of that term.

As the construction is to a great extent based on the experiences with the proton beam at Uppsala it is gratifying to conclude that the dose distributions over a cross section in the region of the lesion and its nearest surroundings are very similar, at the same time as the biologic efficiency also can be expected to be the same.

Acknowledgement

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SUMMARY

The physical conditions for producing minute disc-shaped lesions for functional radiation surgery by means of narrow beam irradiation are discussed. The intention was a treatment procedure for routine clinical use and with high physical and mechanical reproducibility. The possibilities of using high energy electrons, supervoltage roentgen radiation, gamma emitting nuclides or fast neutrons in a technique for routine clinical use were investigated. The radiation of choice taking physical properties, radiation biologic factors and practical circumstances into account was considered to be ^{60}Co gamma radiation. A treatment apparatus containing 179 ^{60}Co sources within a spherical sector of 70° latitude and 160° longitude was constructed.

ZUSAMMENFASSUNG

Die physikalischen Voraussetzungen, um kleine scheibenförmige Läsionen zur funktionellen Srahlenchirurgie unter Anwendung der Feinstrahl-Bestrahlung hervorzurufen, werden diskutiert. Das Ziel war ein Behandlungsverfahren für den klinischen Routinebetrieb und mit hoher physikalischer und mechanischer Reproduzierbarkeit. Die Möglichkeiten, hochenergetische Elektronen, hochvolt Röntgenbestrahlung, Gamma-strahlende Radioisotopen oder schnelle Neutronen bei einer Technik für den klinischen Routinegebrauch zu verwenden, wurde untersucht. Als die Bestrahlung der Wahl unter Berücksichtigung physikalischer Eigenschaften, radiobiologischer Faktoren und praktischer Gegebenheiten wurde die ^{60}Co Gamma-Strahlung befunden. Eine Behandlungsapparatur bestehend aus 179 ^{60}Co Quellen innerhalb eines sphärischen Sektors von 70° Latitude und 160° Longitude wurde konstruiert.

RÉSUMÉ

Les auteurs examinent les conditions physiques permettant d'obtenir de petites lésions en forme de disque pour la chirurgie fonctionnelle par les radiations au moyen d'une irradiation par un faisceau étroit. Le but était de mettre au point une technique de traitement pour l'usage clinique courant présentant une très bonne reproductibilité physique et mécanique. Les auteurs ont examiné les possibilités d'utiliser des électrons de haute énergie, une irradiation par les rayons roentgen à supervoltage et les isotopes émetteurs gamma ou les neutrons rapides par une technique d'utilisation clinique courante. Compte tenu des propriétés physiques, des facteurs biologiques de la radiation et des circonstances pratiques, le ^{60}Co a été considéré comme la radiation de choix. Les auteurs se proposent de réaliser un appareil de traitement contenant 179 sources ^{60}Co situées dans un secteur sphérique de 70° de latitude et 160° de longitude.

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