

EXPERIENCE WITH THE UPPSALA 230 cm CYCLOTRON  
AND PREPARATIONS FOR FUTURE USE IN RADIOTHERAPY

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(References are found on the attached slide copies and in an additional list at the end of the paper).

ACTIVITIES 1952-1976

In 1952 the construction of the 230 cm synchrocyclotron (slide 1) was completed at The Gustaf Werner Institute in Uppsala. This institute is located in the middle of a conglomerate of scientific departments and is less than a kilometer from the University Hospital serving a population of 1.5 million inhabitants. During the years 1957-1968 69 patients were treated with large field, range-modulated proton beams (slides 2a,b and 3a,b).

The first series of patients included only such advanced tumours that curative treatment was judged impossible. Among these were 10 cases of verified recurrences of cervix carcinoma. A total dose of 30 Gy was given in a single fraction with a perineal portal to the pelvic region (slide 4). Fractionated treatment of advanced genital carcinoma was also performed as a second series. We had confidence in our technique and the equivalence of protons and cobalt radiation seemed fairly well established from the biological point of view. Further work was therefore concentrated on cases in which the geometrical advantages of the proton dose distribution could be better exploited. It should be mentioned that in parallel with this radiotherapy project, the proton beam was also used for narrow beam irradiation of intracranial structures (see "Additional Reading" 1-8, 10, 12 and 30).

The next series consisted of 19 patients with cancer of the nasopharynx.<sup>11</sup> A proton dose of 20-40 Gy was given in 2-4 fractions, supplementary to earlier X-ray treatment. Two opposing lateral proton fields were directed on the primary tumour region. The range of the beams was adjusted by a bolus so that overlapping fields gave a full tumour dose in a region of 5 cm around the midline while the dose at the parotides and skin was less than 50% of the tumour dose as indicated in the next slide. By visual and biopsy control the radiation effect on normal and tumour tissue could be studied. No unexpected pathological or clinical findings were made. Twelve out of 19 responded well.

Reference 16 describes the technique used for treatment of malignant glioma by means of a range modulating ridge-filter, absorbers and a bolus made of thin sliding sticks of lucite. Fixation at the auditory canals and the base of the nose was found

to be very effective. The dose was 51 Gy in 10-11 fractions during about one month. One of our 8 patients treated for malignant glioma is still alive. The survival of the other patients was similar to what is expected from other treatment modalities. The brains secured at autopsy were carefully examined. In all brains the tumour cells were altered but viable tumour cells were seen within the treatment volume.

Slide 5 gives the proton dose distribution to a patient suffering from a very advanced thyroid cancer. It was the last patient treated and it illustrates the state of development and the versatility of the technique. By using an appropriate bolus, the whole tumour volume could be treated homogeneously without exceeding the tolerance level of the spinal cord. The same homogeneity of the dose distribution could rarely have been achieved with conventional high energy radiation even if complex multifield arrangements were used. The patient is still alive after 15 years.

The patient material in Uppsala does not lend itself to a statistical analysis since it is small and diverse and most patients were in very advanced stages. Some of the patients are, however, still alive 15-20 years after the treatment.

The following conclusions were drawn in 1968, and are still valid:

1. High energy protons can safely be used for radical radiotherapy.
2. The therapy can be based on experience from conventional therapy since the effects of protons are similar to those of other types of low-LET radiation.
3. The flexibility of the proton field permits an accurate dose distribution in good conformance to generally accepted clinical criteria.
4. There are tumour patients for which proton therapy would obviously be preferable to other types of therapy due to differences in the macroscopic distribution of dose.

The reason for recalling the old situation is that the clinical work in Uppsala paved the way for the later, technically more advanced, studies at Harvard, Berkeley and Moscow. It also forms a basis now that the programme is being resumed in Uppsala. Here, a Swedish national accelerator center is being established based on three different accelerators: the existing tandem van de Graaff, the synchrocyclotron under reconstruction and the CELSIUS ring for the storing and cooling of ions injected from the cyclotron. From the radiotherapy point of view, the Gustaf Werner

cyclotron continues to be the accelerator of major interest. After reconstruction, this new facility, the SFSC-200, will operate both as a synchrocyclotron and as an isochronous cyclotron with  $K=200$  (slides 6-8).

#### THE CYCLOTRON SFSC-200

The improvement programme for the 185 MeV Gustaf Werner synchrocyclotron started in 1977 and aimed at the construction of a three-sector, variable-energy cyclotron. The necessary new buildings (slide 9) were approved and funded by the government in May 1981. Early in 1983 the power supply and control rooms were finished, and in 1984 a 650 square meter area for physics and biomedical research was completed. The present time plan predicts external ion beams from the cyclotron in late 1985. Most of the buildings shown are below ground and closely surrounded by a number of other university buildings. The proximity to other laboratories is an advantage but has, in fact, been a major difficulty and explains much of the special features of the general layout.

Slide 9 also shows the various beam lines under construction. A neutron and nuclide production area, the "spallation crypt", is located on the same level as the cyclotron. All other experimental positions will be about 5 meters above the cyclotron floor and the beam will be brought to this level by two 30 degree magnets. The first target room will be used for neutron production. After this comes the physics area, which is divided into one room with two spectrometers, one 135 degree ion spectrometer and one pair spectrometer and finally a room for low-background gamma measurements. The biomedical research will be supplied with four different beam lines for experimental and clinical research.

The layout of the experimental and therapy areas is given in slide 9. The cyclotron is located 10 meters underground and the new areas are about 5 meters above the cyclotron level. The small rectangular area next to the right of the cyclotron was the only laboratory that existed before. The new biomedical area is shown in the upper right corner and two treatment rooms are planned at this level, one for narrow beams less than 3 cm in diameter, and one for broad beams up to 30 cm in diameter. Next to the treatment area is an old building that will hold some patient-related areas.

The reconstructed cyclotron will be able to operate either with frequency modulation (FM) or at fixed frequency (CW). The FM mode must be used for protons in the energy range of 110 to 200 MeV, while protons of lower energy and heavier particles can be accelerated in CW mode. Slide 8 shows the energies obtainable for various particles. The  $K$  value of the cyclotron has increased

from 185 MeV to 200 MeV by the modified pole geometry. Protons in the very highest energy range (i.e., above 185 MeV) will be reached only at reduced modulation frequency due to the increased bandwidth requirements.

The design philosophy for the field was given by Holm and Renberg (1978). A three-sector polegap geometry which is now installed was studied in an extensive set of field measurements and orbit calculations on a 1:4 model. The field of the full scale magnet has been mapped over the useful range of the cyclotron, from 2.5 to 17.3 kGauss.

The acceleration will be performed by two identical RF systems of the "master oscillator + power amplifier" type in both CW and FM modes. The amplifier chain of each system consists of a 1 kW, a 10 kW and a 100 kW stage. The systems are tunable from 12 to 24 MHz for operation on the harmonics number 1, 2, 3 and 4. The dee electrodes have an azimuthal width of 72 degrees at the center and 42 degrees at extraction. Built around a strong but light, supporting structure of stainless steel and clad by sheet copper, they are cantilevered from the vacuum feedthrough and tuned by moving shorts in air. The equivalent dee capacity is about 315 pF at 24 MHz. The natural quality factor is reduced in FM mode from about 200 to 100 by connecting a 40 kW resistor in parallel to the dee stem. The maximum dee voltage is approximately 50 kV in CW mode and 12 kV in FM mode. The final amplifiers (capable to withstand an anode dissipation of 100 kW in the FM mode) are inductively coupled to the dee resonators and move together with the dee tuning shorts on a rail.

The cyclotron will initially be equipped with an internal PIG ion source with a double arc chimney for operation in both first and second harmonic with the same geometry. Due to the difference in dee voltage between FM and CW operation, different sized geometries have to be used. There are also plans for external injection. A special ion source room has been built for this purpose outside the cyclotron hall.

Beams will be extracted from the cyclotron with either regenerative or precessional techniques. The two main deflecting elements are an electrostatic deflector and an electromagnetic channel (EMC). A passive focussing channel will be placed in the fringe field about 20 degrees downstream from the exit of the EMC.

Regenerative extraction will be used when operating in FM mode and in some cases of first harmonic CW operation when the energy gain per turn is low. A peeler and a regenerator will then be inserted.

The vacuum chamber is designed with a prevacuum part housing the epoxy-moulded trim coils. The construction material in the

chamber is an aluminum alloy. In the high vacuum region most of the seals consist of soft aluminum wire. Conventional pumping by diffusion pumps backed by roots pumps is foreseen for the initial operation. The calculated ultimate vacuum lies in the  $10^7$  Torr range.

The cyclotron will be computer-controlled with distributed microprocessors, organized at three levels. At the lowest level the processors will be integrated in the equipment serving both local control and communication with the higher level. The processors in the middle level will supervise the different systems such as magnet, RF and so on. The main computer (TMS 990-12) is connected to the control console and helps the operators to set and read the data bases in the lower systems.

In slide 8 the expected performance of the reconstructed cyclotron is summarized, assuming an internal ion source. Estimated current for heavy ions are based on results from other cyclotrons. When operating with frequency modulation the phenomenon most likely to limit the current will be space charge close to the centre of the cyclotron. Based on a simplified calculation of that limit the maximum external proton current in the high energy range will be around  $10 \mu\text{A}$ . For CW acceleration of P and D beams, assuming conservatively 80% extraction efficiency, a maximum septum power of 1 kW will permit a  $40 \mu\text{A}$  external beam. For heavier ions the ion source will be the limiting factor.

The  $\Delta E$  values given for the FM case have been calculated assuming radial amplitudes less than 4 mm and a dee voltage for 185 MeV protons of 12 kV. Both the radial amplitudes and the accelerating voltage influence the energy spread of the external beam in the method gives smaller values.

In FM operation the beam will be pulsed with a maximum frequency of 1000 Hz. For injection into the CELSIUS ring, and for radiobiological studies, it may be desirable to have short pulse lengths. The number of protons in a beam pulse will be up to  $6 \cdot 10^{10}$ . With normal setting of the cyclotron in "short burst operation", the bucket half width will be 25  $\mu\text{s}$ , the shortest pulse length possible from the cyclotron with a filled bucket. Due to the conditions for particle capture at the center of the cyclotron, however, the bucket will in practice be empty at the center. Cyclotron orbit studies have shown that the unfilled bucket will cause the beam pulse to be shortened, typically from 25 to 8  $\mu\text{s}$ . A further reduction of the pulse length is possible by adiabatically increasing the accelerating voltage in the cyclotron and at the same time the rate of frequency change. For example, with a doubling of the dee voltage during a short time prior to extraction (which may be done without excessive power loss)  $df/dt$  can be increased by a factor 2.9 without loss of particles. This will cause a further reduction of the pulse length to about 3  $\mu\text{s}$ .

In this example, the time for capture at the cyclotron center was 12-17  $\mu$ s. Thus the cyclotron is expected to bunch by a factor 5.

#### COLLABORATION WITH ITEP 1976-1985

Since 1976 there has been a collaborative programme between the Institute of Theoretical and Experimental Physica (ITEP) in Moscos and the Gustaf Werner Institute on physical, radiobiological and technical aspects on the use of proton beams in medicine. Considerable experience in the development of proton therapy methods has accumulated at ITEP and at the Gustaf Werner Institute during this time. Methods of treatment planning, radiobiological research and labelled compound productions have improved. Among joint research projects may be mentioned:

1. Proton beam transport and control.
2. Production of short-lived radionuclides and labelled compounds such as  $^{11}\text{C}$ -methionine and  $^{11}\text{C}$ -glucose which are used for tumour studies in patients and animals with the positron emission tomograph in Uppsala.
3. Intercomparison of methods for dosimetry. In this context special attention has been paid to semi-conductors. In collaboration with Therados Company, Uppsala, a silicon detector was developed that showed dose rate independence up to a dose of 0.2 Gy per pulse suitable for the high pulse dose rate of the ITEP accelerator.

We have had the opportunity to exchange clinical experiences also with the groups in Moscow and Leningrad and at Dubna (slide 21). At Dubna about 30 patients with cancer of the oesophagus, lung or larynx have been treated with protons. A major reconstruction of the accelerator and the radiotherapy sites is performed allowing treatment with protons, neutrons and pi-mesons in separate rooms. The treatments have not yet been reinstited.

At Gatchina<sup>17</sup> only therapy with narrow beams using cross-fire techniques has been given. Thus, more than 12 cases of functional disorders of the brain and more than 60 pituitary irradiations for ablative purposes of patients with cancer of the breast and of prostate have been performed. About 100 patients with pituitary adenomas have also been treated.

At ITEP patient irradiations have been carried out since 1969. Radiotherapy can be given independently of simultaneous physical investigations. Up to the end of 1981, 575 patients had been treated at this facility with one single treatment room with two irradiation sites, one for broad beams and one for stereotactic radiosurgery. Recently two new treatment rooms have been added and the patient load is expected to increase considerably.

The clinical results appear to be similar to those achieved at Harvard and Berkeley. It is a common understanding, however, that the possible merits of proton radiotherapy over conventional radiation can only be demonstrated through randomized trials. It is also generally agreed that a randomized comparison is only allowed when the investigator cannot predict the outcome of the trial. The only known difference between high energy protons and other types of conventionally used radiations is the macroscopic dose distribution. Very large groups of patients must be included to have a chance to detect a significant difference in result. We therefore undertook a design study of a large scale proton treatment facility in Uppsala in order to evaluate the clinical, technical and economical prospects. The potential patient load was estimated from tumour incidence tables and the number of patients treated curatively with radiotherapy. About 1/4 of the patients were found to gain from being treated with protons. Assuming an eight million population, about 200 proton treatments per day should be needed provided conventional fractionation schemes were followed and all radiotherapy was given with protons. Fixed proton beams were supposed and the patients should be treated in a supine position. It was estimated that four fixed beam directions should be needed. The beam directions and the relative treatment loads are shown in slide 10a. With five treatment rooms, the requirements of 200 treatments per day should be satisfied. Separate facilities for radiosurgery and radionuclide production should also be provided. A model of the facility is shown in slide 10b. The total cost of the building, cyclotron beam transport and computer equipment was estimated and it was found to be comparable to that for a clinic with five electron accelerators. The facility for radiosurgery and radionuclide production may even make the balance in favour of the cyclotron facility. There are no plans for building such a large scale facility in Sweden. It would probably be more favourably located in a densely populated large metropolitan area, as is now discussed in the U.S.S.R. In Uppsala only a restricted number of patients will be treated at the new facility. The primary aim is research and technical development.

#### PLAN FOR THE WORK AT SFSC-200

So far, most attention has been paid to the clinical aspects on the use of proton beams in oncology and surgery. In parallel with the above investigations, however, a scientific program evolved with weight put upon basic radiation research in which the various beams and radionuclides from the cyclotron were exploited. Its main elements are various aspects on the radiation response of mammalian cells and tissues, quantification of effects in biochemical and pathophysiological terms, and the search for efficient effect-modifying principles.

One major task of technical development prior to the clinical use of SFSC-200 seems to be particularly relevant, in the present context. Several steps towards optimization of the depth dose distribution with protons have been conceived following the ideas of Drs. A. Koehler and M. Goitein, et al., at Harvard. We are also interested in "spot scanning" with variable modulation and compensation as described by Kawachi, Kanai and others. We are contemplating the use of the latter technique incorporated in a gantry system, as illustrated in slides 11 and 12. It would give a fully isocentric proton delivery system with a flexible collimator by means of a  $60^\circ$  bending magnet, a quadrupole lens and a cross plane steering magnet, a  $143^\circ$  bending magnet. Inside this magnet there will be a scattering foil to assure uniform proton coverage of the elementary beam and mask any internal inhomogeneity which may be present in the beam from the accelerator. The location of the foil and the exit angle of the magnet are chosen such that the beam is essentially parallel when leaving the magnet. This pitch will allow a  $180^\circ$  rotation of the gantry which is already constructed.

Slide 12 shows a close up of the scanning magnets, the dual wedge range shifter and the flexible collimator. In order to make the size of gantry reasonable there is one stationary scanning magnet and one pivoting around the virtual scanning center of the first scanning magnet. This solution will allow  $30 \times 30$  cm large fields with an effective SSD of 100 cm using conventional magnet technology. All three scanning motions and the flexible collimator should be accurately coordinated and controlled by the same computer. The second scanning magnet pivots mechanically so that its median plane coincides with the direction of the proton beam as it leaves the first scanning magnet. At present we have no funds for the construction of this gantry system and so, when treatments are started again at the end of next year, the work will first focus on the narrow beam for treating eye tumours, pituitary adenomas and other small intracranial targets.

The mentioned development does, indeed, put rigorous demands on the beam handling system. At first glance the uniformity of the beam cross sections seems to represent a problem, since the cross section of the "raw" beam may be very inhomogeneous. It was easily solved, however, already in the previous installation, by letting the beam describe a rectilinear Lissajou pattern (slide 13). (A thin scatter foil was used to soften the beam structure.) This technique for beam homogenization by pencil sweeping has the obvious advantage that it minimizes beam intensity losses and production of contaminating secondary radiation. In fact, the system has turned out to be reliable and permits excellent homogeneity without sophisticated electronic control. A modified version is now being conceived based on computer control of a more flexible beam-sweep system (slides 14-20). Reference is made to a study done for the ITEP, Moscow, where 200 MeV proton pulses are

tapped at a frequency of 0.5 Hz from the 10 GeV synchrotron. Under such conditions, a relatively small number of pulses are delivered in a typically therapeutic sitting, such as 300 in 10 minutes, and the beam sweep pattern has to be optimized for maximum homogeneity of flux density.

#### OBSERVATIONS AND CONCLUSIONS

We observe that medium energy protons have largely been accepted as a potentially useful treatment modality in oncology and neurosurgery, also in a large-scale clinical context. Their social impact is still to be seen, however, there is still no hospital-based proton-beam facility installed or projected. The main reason for this inappropriate situation seems to be that proposed installations are considered fancy, clumsy and too expensive.

Now, when computerized tomography (CT, NMR, PET) create new rationales and possibilities for precision in radiotherapy and radiosurgery, the challenge is increasing: new, convenient technical concepts have to be sought!

The renovated Uppsala cyclotron, the SFSC-200, may serve as a convenient test facility in the present phase of development.

#### ACKNOWLEDGMENT

Described developments at the Uppsala cyclotron have been supported by the Knut and Alice Wallenberg Foundation, the Swedish Cancer Society, the Swedish Medical Research Council, the Swedish Natural Science Research Council, the National Swedish Board for Technical Development, and the Swedish Academy of Engineering Sciences.

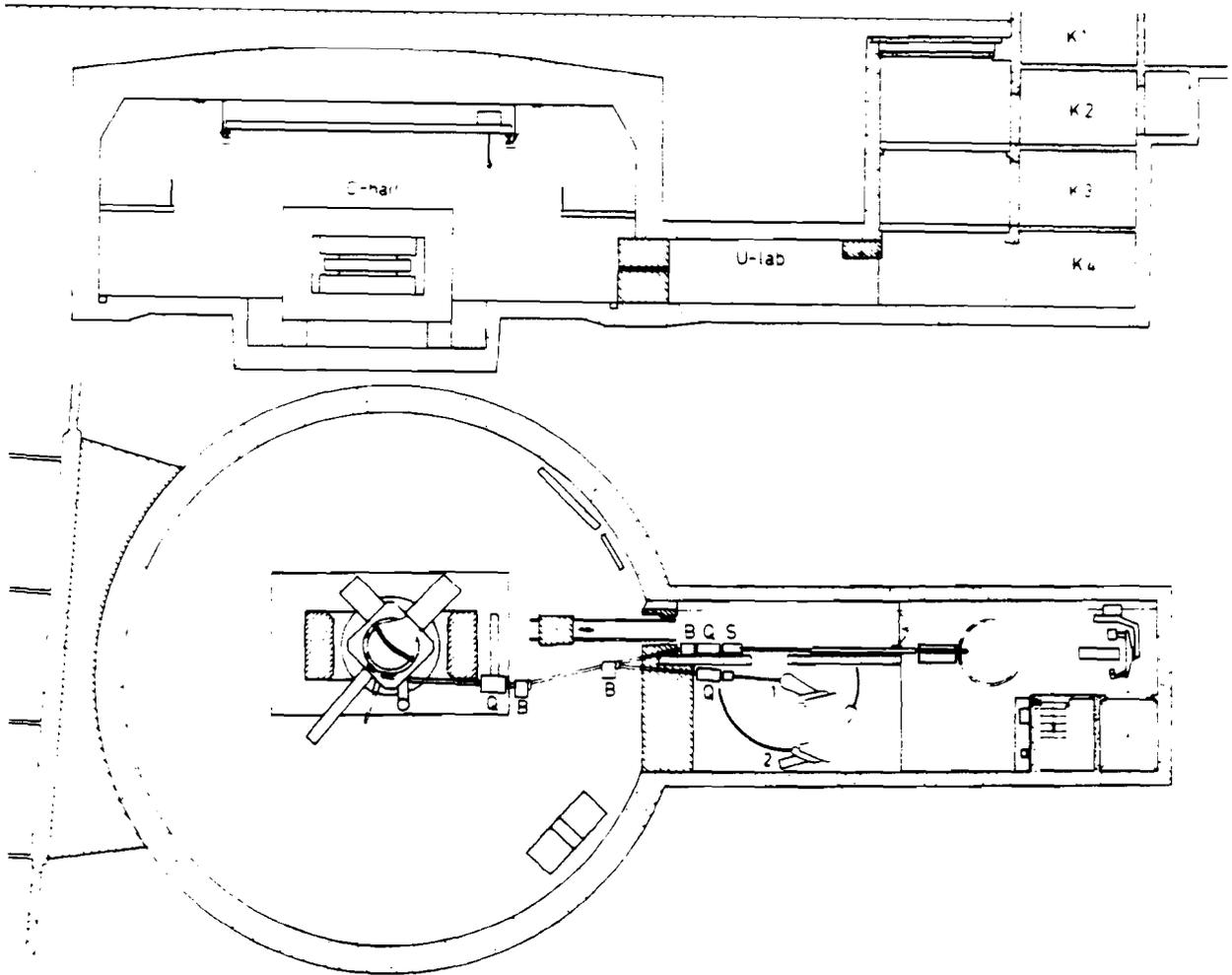
## ADDITIONAL READING

In addition to references given on the attached slide originals, the following papers contain information of relevance in the context of proton radiotherapy and other medical applications of medium energy particle accelerators:

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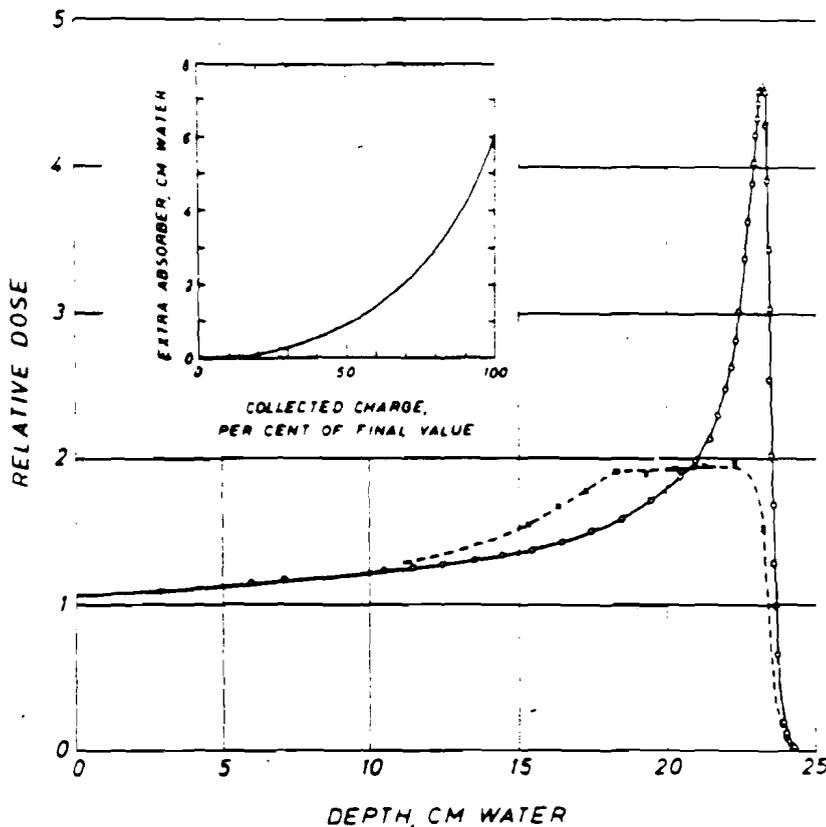
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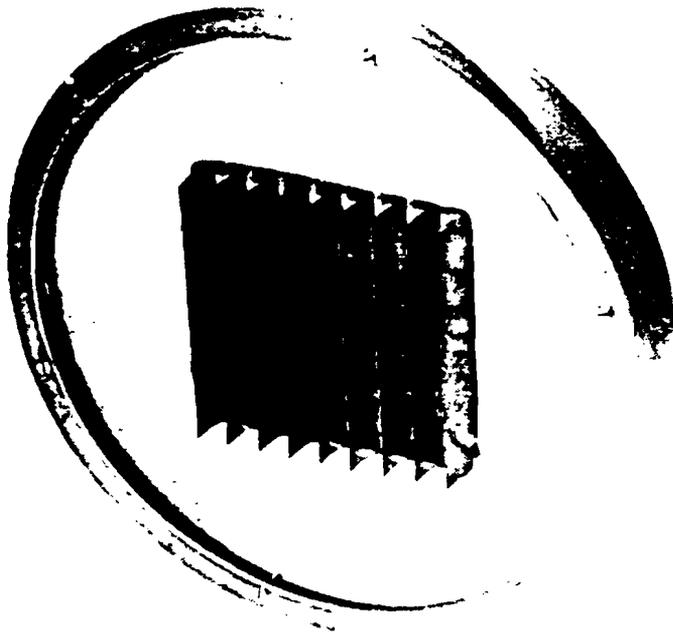


Slide 1: Plan of the cyclotron hall and adjacent experimental rooms in operation 1956-1977. The external beam laboratory ("U-lab") was used for physical and biomedical experiments as well as for clinical applications.

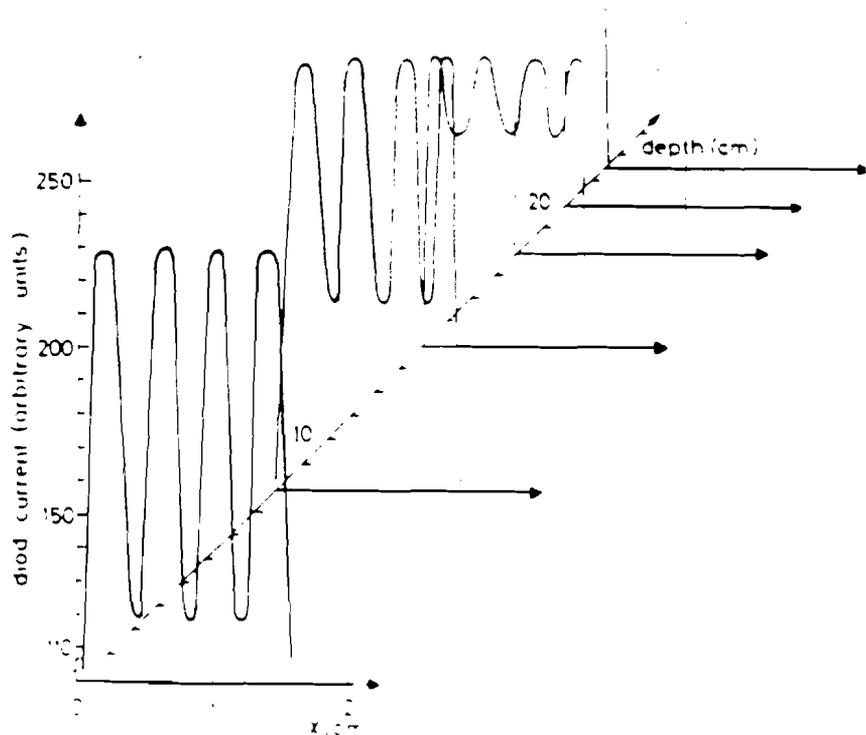
Slides 2a and 2b:  
 Transformation on the Bragg peak. Variation of the water absorber in front of the target was performed, during irradiation, according to the curve in the inset diagram. The original (—) and the transformed (-----) depth-dose curves are shown. Points of measurements (x) on a depth-dose curve obtained by the use of a ridge filter (Slide 3) are indicated. The profile of the ridges was determined by the shape of the curve in the inset diagram, 1 cm water being equivalent to 0.18 cm brass. (Courtesy Brit. J. Radiol.)



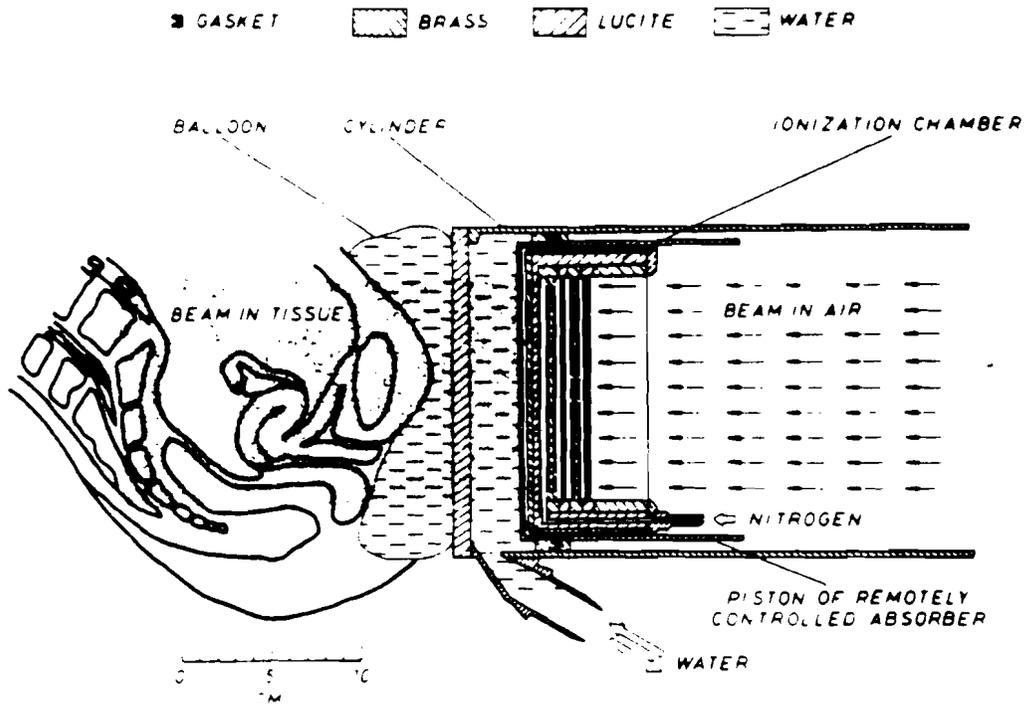
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Slide 3a: A ridge filter designed for 135 MeV protons. Its characteristic profile and effects on the depth-dose distribution are designed on Slide 2a.



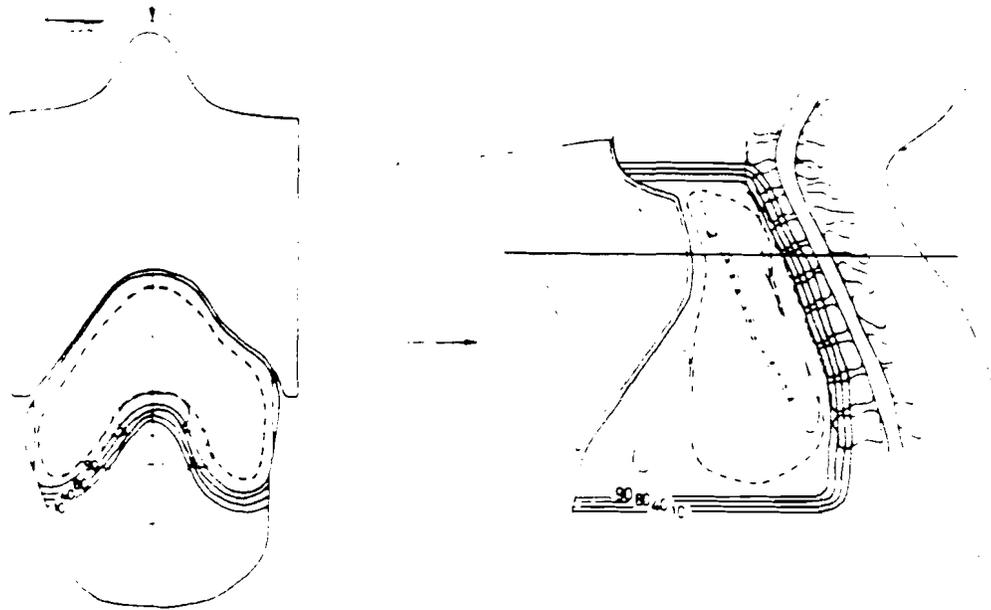
Slide 3b: The ridge filter affects the depth-dose distribution by introducing pre-calculated differences in the particles' range of penetration. The ridge structure, reflected in the lateral distribution of dose at shallow depths, becomes of little importance in the region of the "Bragg plateau". This distribution of dose was measured with a small signal diode at linear response by Dr. H. G. Rikner, Uppsala.



Slide 4: Section through the apparatus in Figure 4 arranged for irradiation of tumours in the pelvis by a spread-out Bragg peak. The piston controlling the varying thickness of the water absorber is shown at a moment when its position gives maximum penetration of the beam.

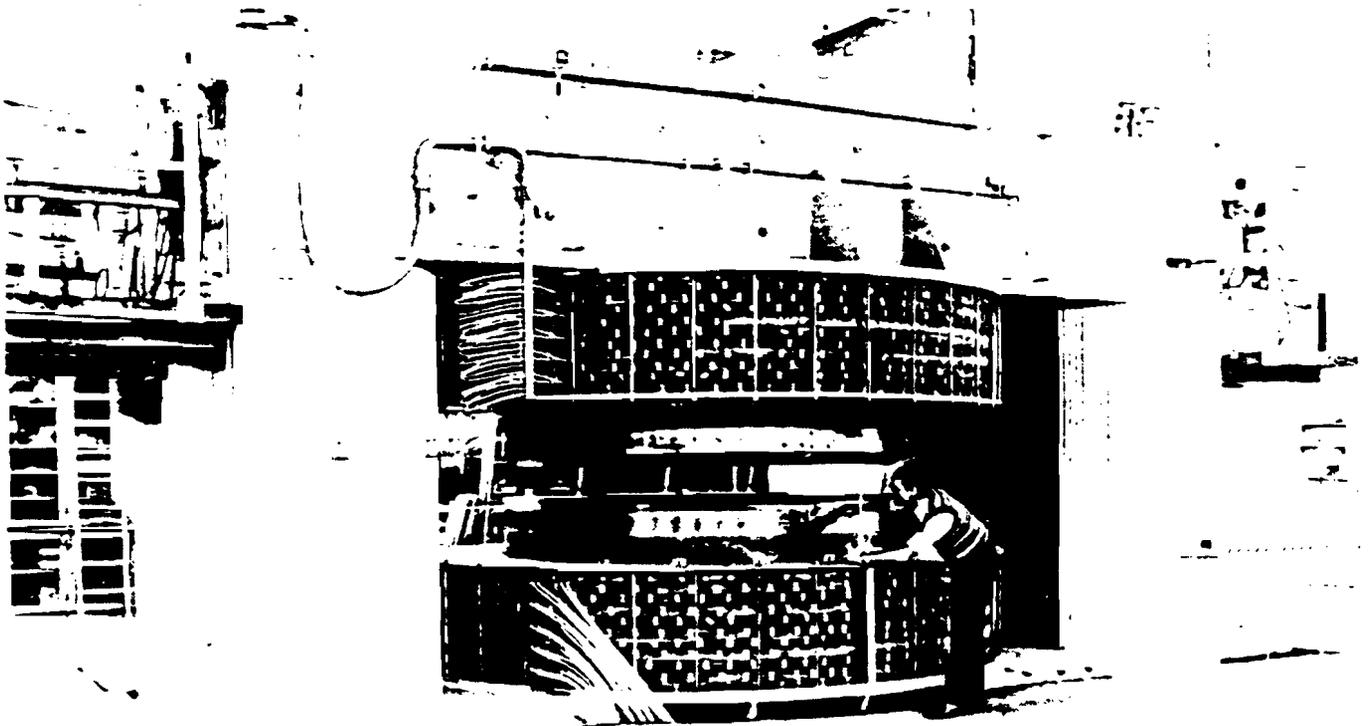
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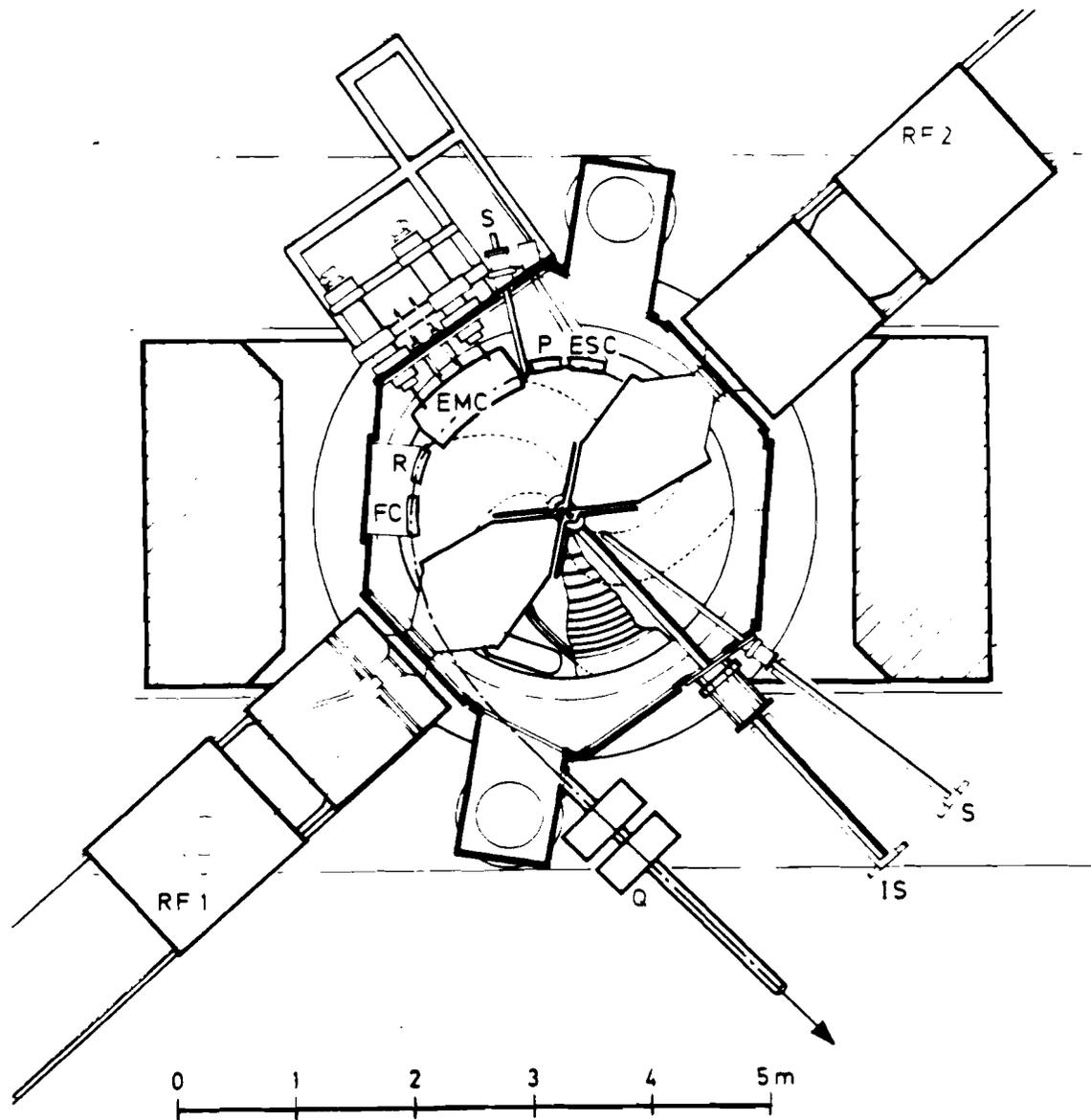
Slide 5: Distribution of dose in a single field of 185 MeV protons tailored to a target volume (-----) containing an infiltrating thyroid carcinoma. (Courtesy Atomkernenergie)

S. Graffman: Thesis, Umea University (1975). Referred to in: S. Graffman and B. Larsson, High-Energy Protons for Radiotherapy - A Review of Activities at the 185 MeV Synchro-Cyclotron in Uppsala, Atomkernenergie 27: 148 (1976).



Slide 6: A sector-focusing synchrocyclotron, the SFSC-200, is being constructed at the Gustaf-Werner Institute on the basis of the magnet of the 230-cm synchrocyclotron.

S. Dahlgran, A. Ingemarsson, S. Kullander, B. Lundstrom, P. U. Renberg, K. Stahl, H. Tyren, and A. Asberg: Conversion Studies for the Uppsala Synchrocyclotron, in "Seventh International Conference on Cyclotrons and Their Applications, Zurich 1975", W. Joho, ed., Birkhauser Verlag, Basel (1975).



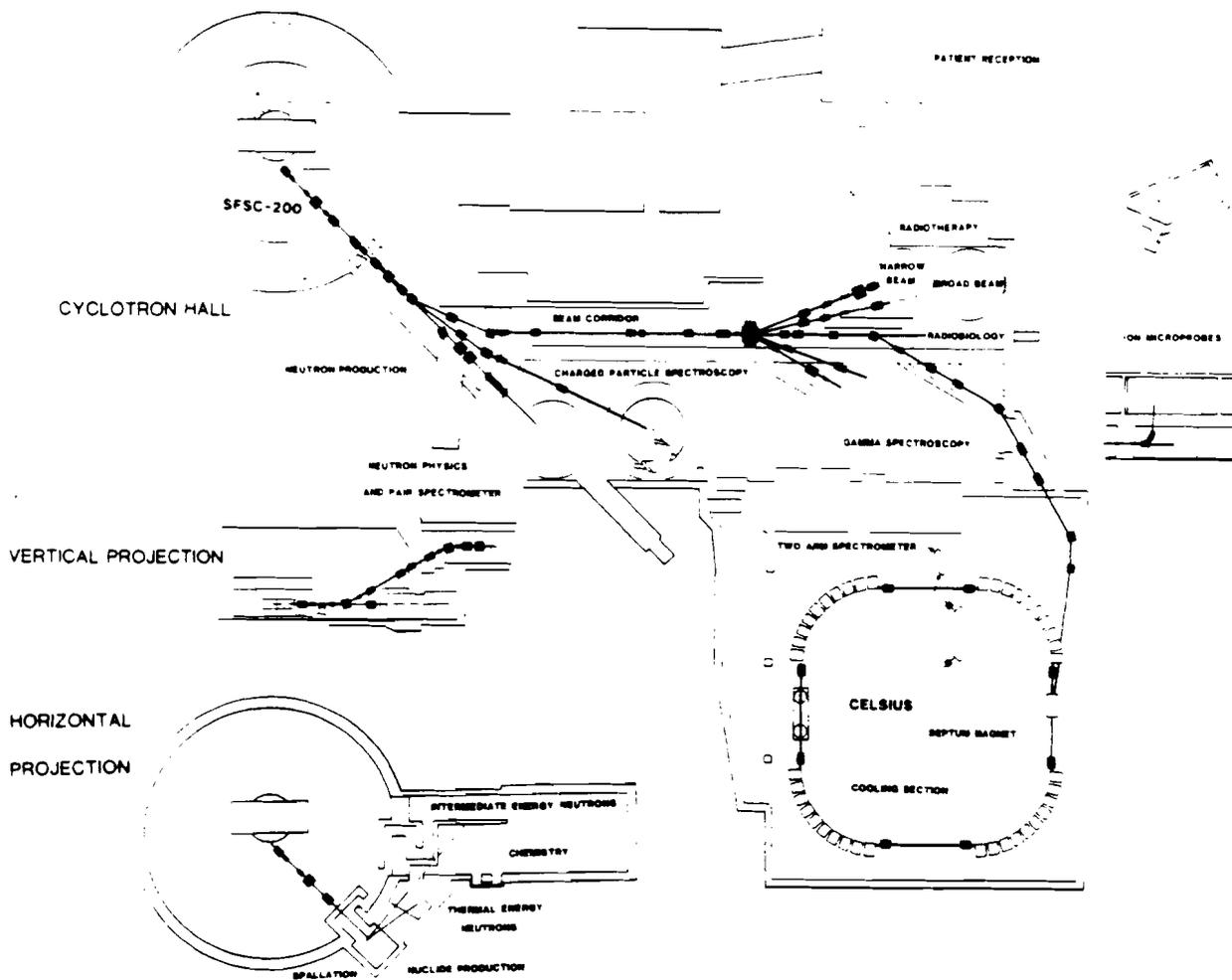
Slide 7: The Cyclotron SFSC-200. The reconstructed cyclotron will be able to operate either with frequency modulation or at fixed frequency. The FM mode must be used for protons in the energy range of 110 to 200 MeV, while protons of lower energy and heavier particles can be accelerated in CW mode.

A three-sector polegap geometry is now installed. The field of the full scale magnet has been mapped over the useful range of the cyclotron, from 2.5 to 17.3 kGauss. The acceleration will be performed by two identical RF systems of the "master oscillator + power amplifier" type in both CW and FM modes.

Ion	Energy (MeV)	Acc mode	Extr meth	Energy res %	Hor emitt mm-mrad	Estim intens (eμA)
P	110-200	1-FM	Reg	0.22	6-8	10-1
P	45-110	1-CW	Reg	0.5	4-5	40
P	45-110	1-CW	Prec	0.17	20	40
$^3\text{He}^{2+}$	250-267	1-FM	Reg	0.22	6-8	2
$^3\text{He}^{2+}$	137-250	1-CW	Reg	0.5	4-5	20
$^3\text{He}^{2+}$	35-137	2-CW	Prec	0.17	20	20
D	25-100	2-CW	Prec	0.17	20	40
$^{12}\text{C}^{4+}$	133-267	2-CW	Prec	0.17	20	5
$^{16}\text{O}^{5+}$	167-312	2-CW	Prec	0.17	20	10
$^{20}\text{Ne}^{7+}$	223-490	2-CW	Prec	0.17	20	0.1

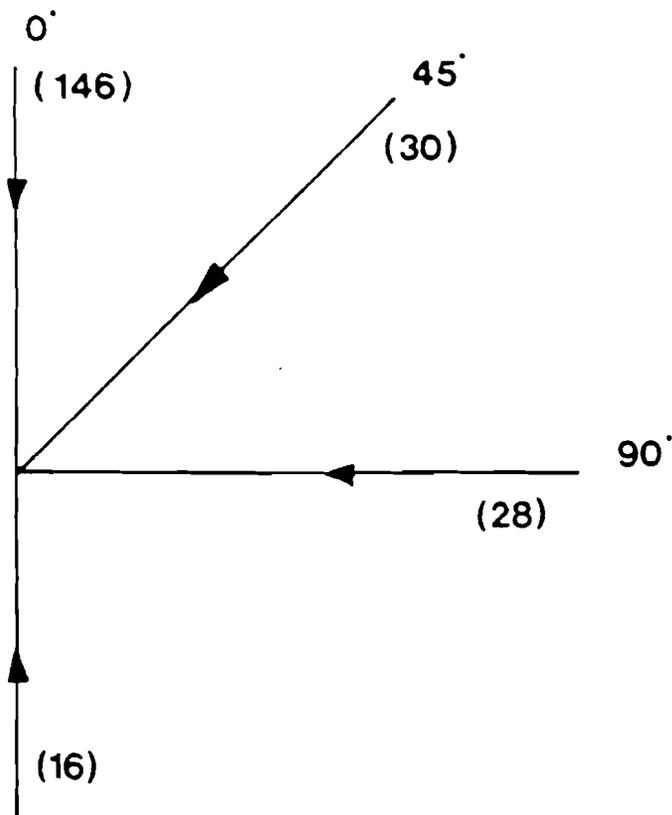
Slide 8: The expected performance of the reconstructed cyclotron SFSC-200 assuming an internal ion source. Estimated currents for heavy ions are based on results from other cyclotrons.

Slides 7 and 8, as well as the technical data on SFSC-200, in the text are from S. Holm, A. Johansson and the GWI cyclotron and CELSIUS groups.



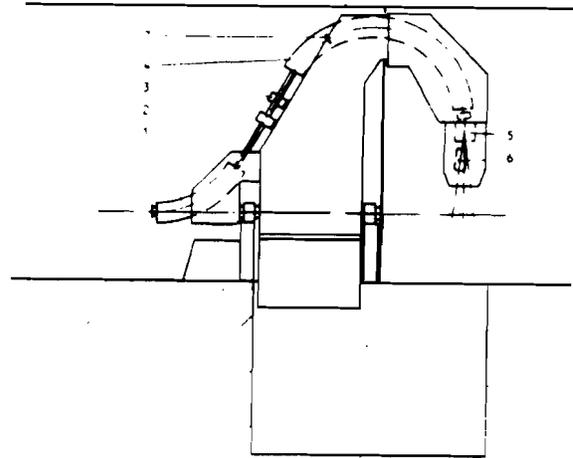
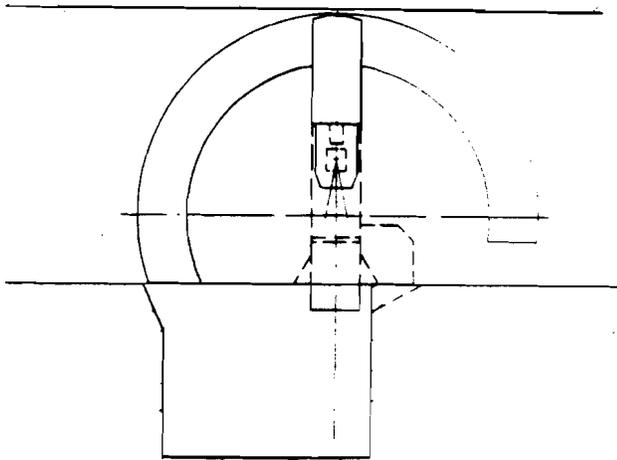
Slide 9: Outline of the various beam lines planned. A neutron and nuclide production area, the "spallation crypt", is located on the same level as the cyclotron. All other experimental positions will be about 5 meters above the cyclotron floor and the beam will be brought to this level by two 30 degree magnets. The first target room will be used for neutron production. After this comes the physics area which is divided into one room with two spectrometers, one 135 degree ion spectrometer and one pair spectrometer, and finally a room for low-background gamma measurements. The biomedical research will be supplied with four different beam lines: broad and narrow beams as well as a micro-beam.

There is also a beam transport line from the cyclotron to CELSIUS, over 100 meters long. Two switching magnets will allow short injection intervals into CELSIUS to minimize interference with other beam users, independent of what target position they may use.



### TREATMENT ANGLES

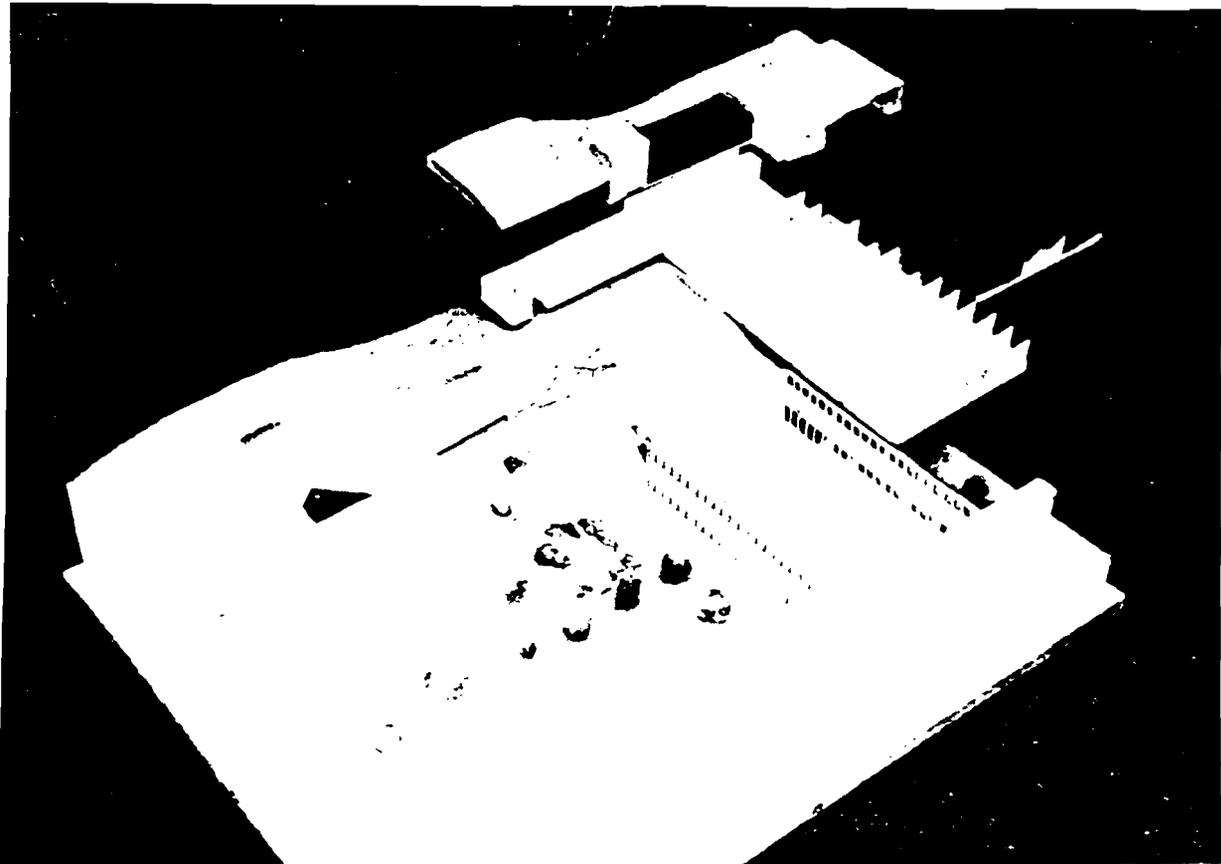
Slide 10a: A study was made of different patient categories that may preferably be treated at a hypothetical Swedish proton therapy center. The diagram indicates the preferred beam directions and the corresponding numbers of patients per day.



Slide 11: Several steps towards optimization of the depth dose distribution with protons have been conceived. Such a technique may be incorporated in a gantry system which is illustrated here and in the following slide.

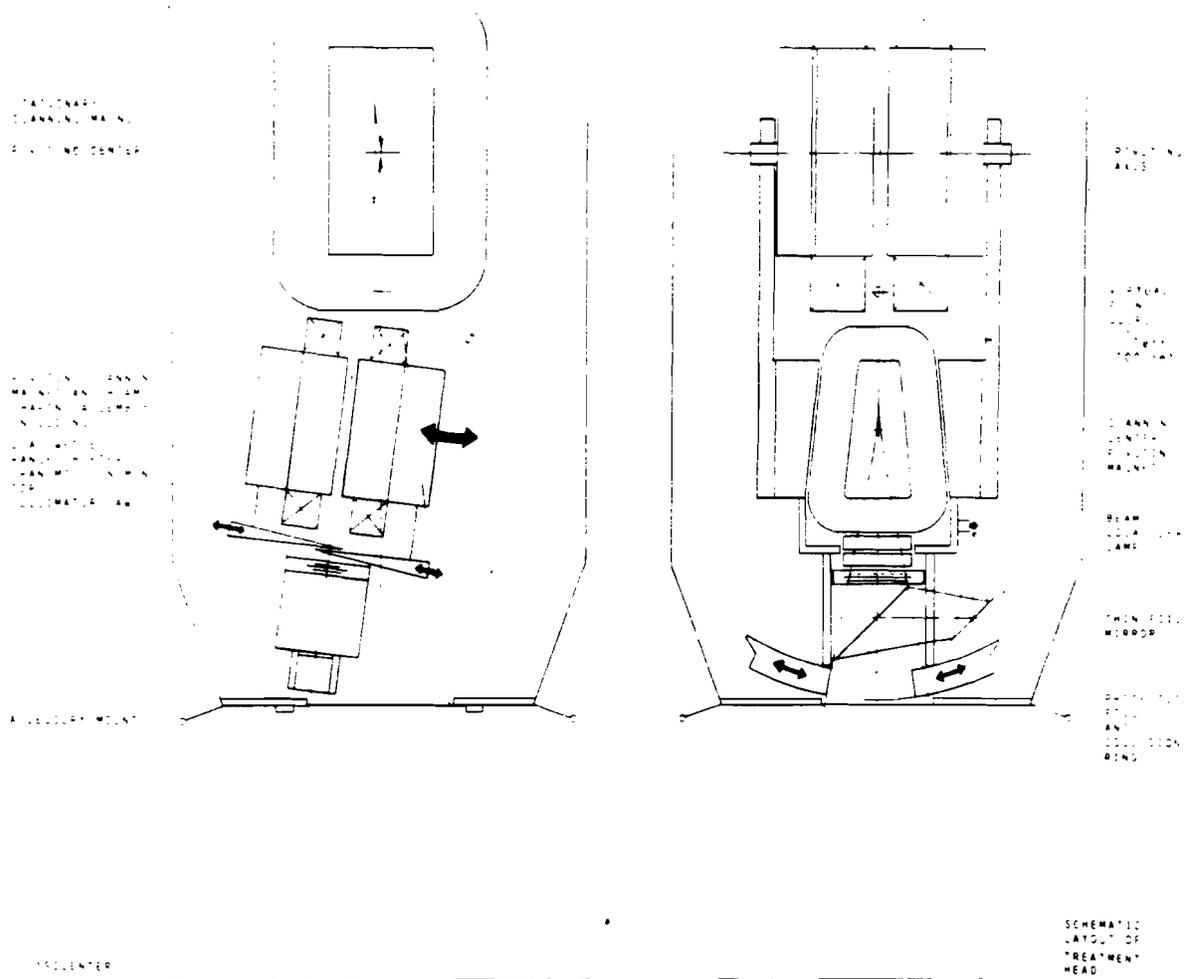
It would give a fully isocentric proton delivery system with a flexible collimator by means of a 50 degree bending magnet, a quadrupole lens and a cross plane steering magnet, a 143 degree bending magnet. Inside this magnet there will be a scattering foil to assure uniform proton coverage of the elementary beam and mask any internal inhomogeneity which may be present in the beam from the accelerator. The location of the foil and the exit angle of the magnet are chosen such that the beam is essentially parallel when leaving the magnet.

From S. Graffman, B. Larsson and A. Brahme, to be published.

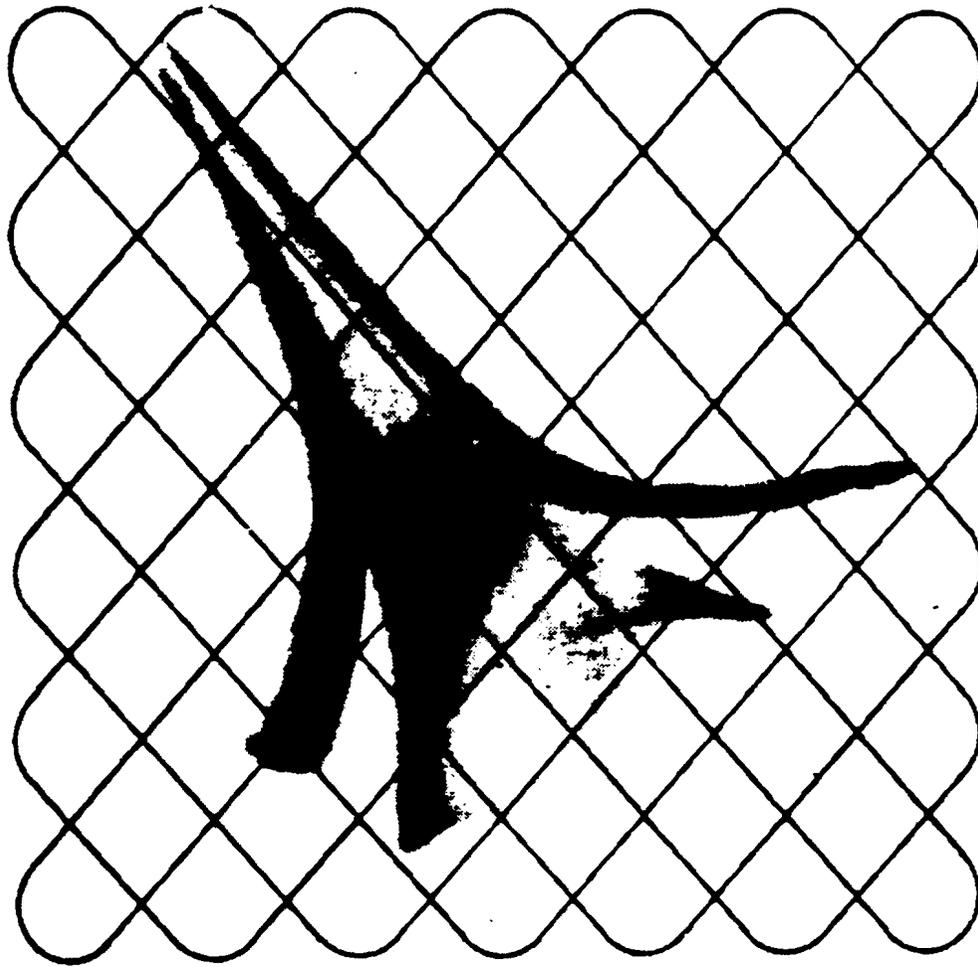


Slide 10b: The architect's model of the proton therapy center constructed from principles outlined in slide 10a. The beam transport tunnel is indicated, leading from the cyclotron cave to five treatment rooms and additional facilities.

From S. Graffman, B. Jung and B. Larsson: Design Studies for a 200 MeV Proton Clinic for Radiotherapy, in "Proc. Sixth International Cyclotron Conference, Vancouver 1972", American Institute of Physics (1973).



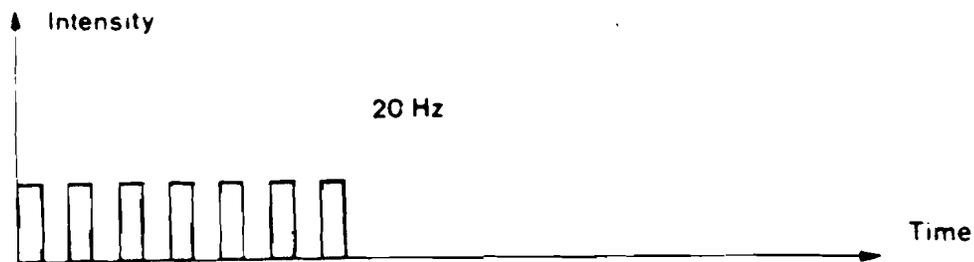
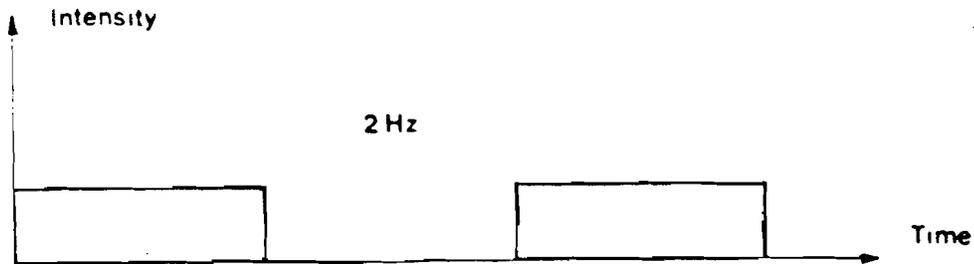
Slide 12: Close up of the scanning magnets in Slide 11, the dual range shifter and the flexible collimator. In order to make the size of gantry reasonable there is one stationary scanning magnet and one pivoting around the virtual scanning center of the first scanning magnet. This solution will allow 30x30 cm large fields with an effective SSD of 100 cm using conventional magnet technology. All three scanning motions and the flexible collimator are accurately coordinated and controlled by the same computer. The second scanning magnet pivots mechanically so its median plane coincides with the direction of the proton beam as it leaves the first scanning magnet.



1cm

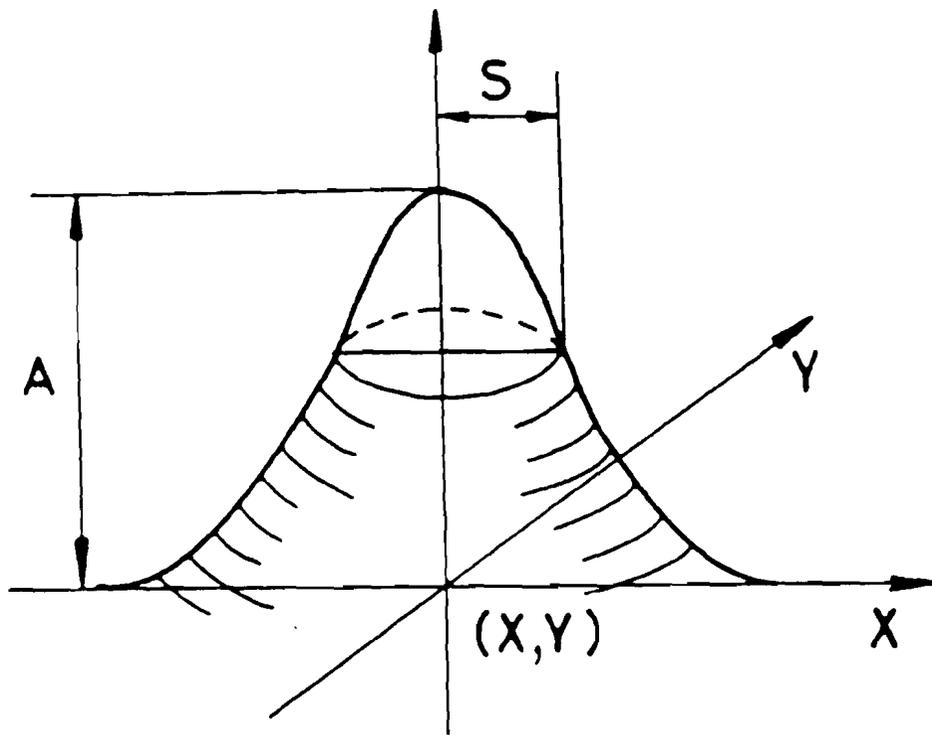
Slide 13: From early experiments with 185 MeV protons: photographic record of the cross section of an extremely inhomogeneous beam pencil, as it appeared in the biomedical target area. By scanning the beam pencil over a 2 cm wide, field-defining collimator as indicated by the line pattern, excellent homogeneity of flux density was achieved in the collimated beam.

From B. Larsson, L. Leksell, B. Rexed and P. Sourander: Effects of High Energy Protons on the Spinal Cord; Acta Radiol. 51: 52 (1959).

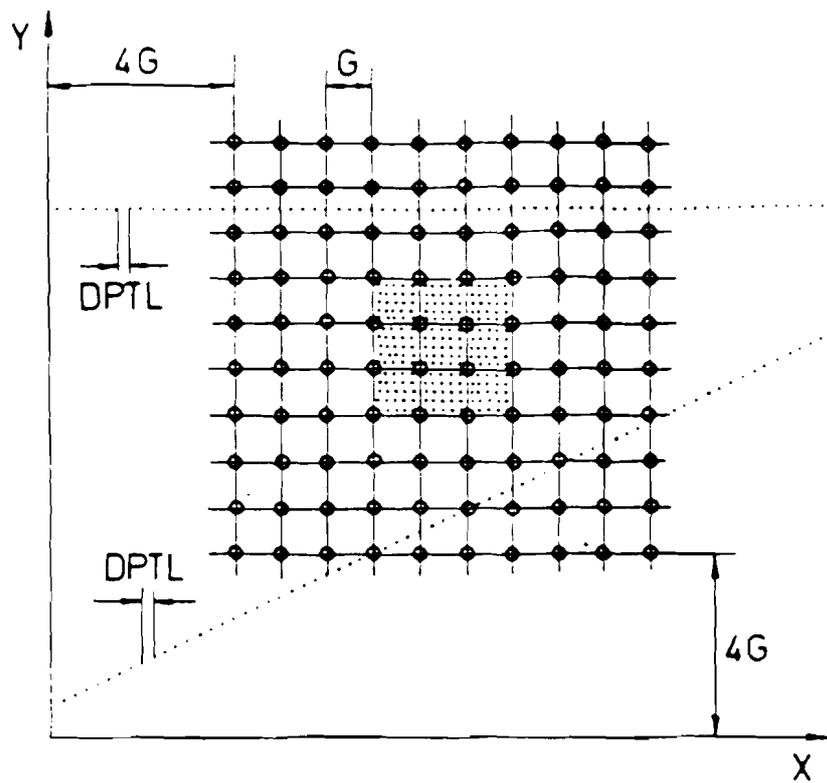


Slide 14: Illustration of prerequisites for beam homogenization by beam pencil sweeping. This is an idealized representation of two trains of "macroscopic" beam pulses as they would appear in a single treatment room at, respectively, a synchrotron operating at a repetition frequency of 2 Hz (above) and a cyclotron operating at several hundred Hz (below); in the latter case the beam is thought to be modulated at 20 Hz by a beam switching magnet (see text).

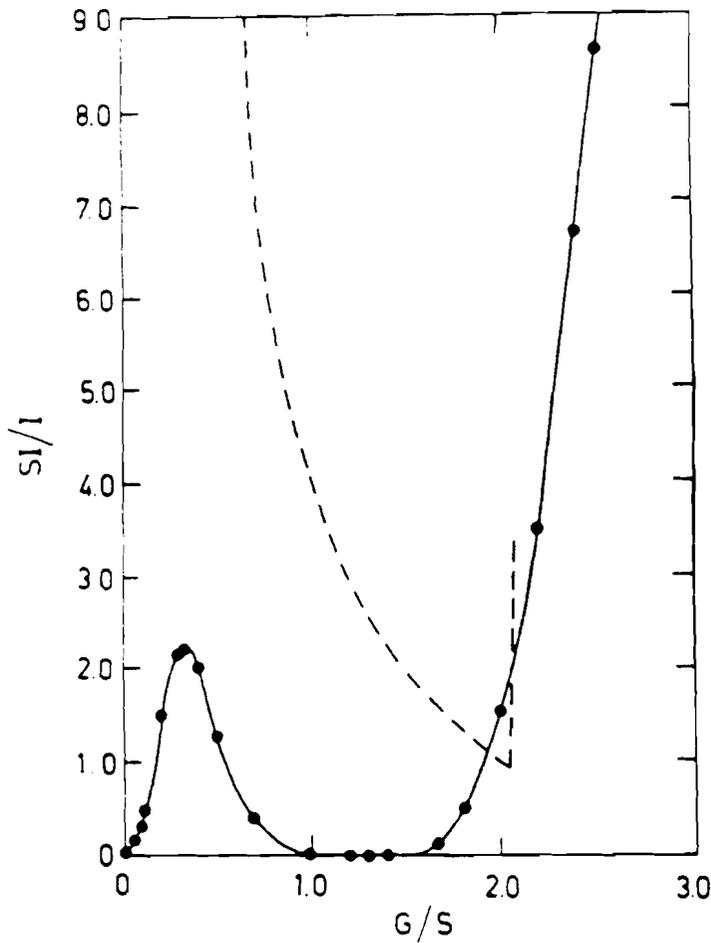
Slides 14 and 15-18 from S. I. Blokhin, V. M. Breev, J. Carlsson and B. Larsson: Homogeneous Transverse Distributions of the Accelerated Ions at Dose Fields for Radiotherapy, in "Proceedings of the First International Seminar on the Uses of Proton Beams in Radiation Therapy, Moscow, Dec. 6-11, 1977", Vol. 1, p. 106, M. I. Lomakin, ed., Atomizdat, Moscow (1979).



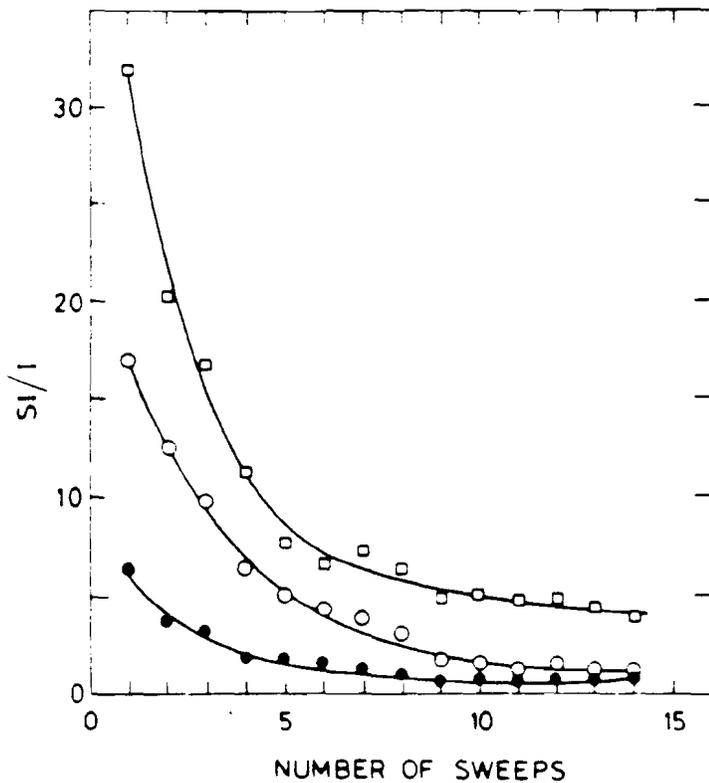
Slide 15: This and the following three slides consider the conditions for homogenization by step-wise scanning of a narrow beam pencil, as simulated in a computerized model. The cross-section of the beam, in the  $x,y$ -plane, is represented by a Gaussian distribution of fluence, typical for a well-collimated beam scattered by a thin foil.



Slide 16: Distribution of beam pulses in the x,y-plane.



Slide 17: Result of computerized simulation of step-wise beam pencil scanning in accordance with Slides 15 and 16. The relative spread of the flux density ( $SI/I$ ), within the field demarcated and analyzed, is given as a function of the ratio  $G/S$ , assuming that all parameters,  $X$ ,  $V$ ,  $S$  and  $A$  are unaffected by stochastic spread. Excellent homogeneity is achieved for  $G/S = 1$  to  $1.5$  after one or several complete sweeps.

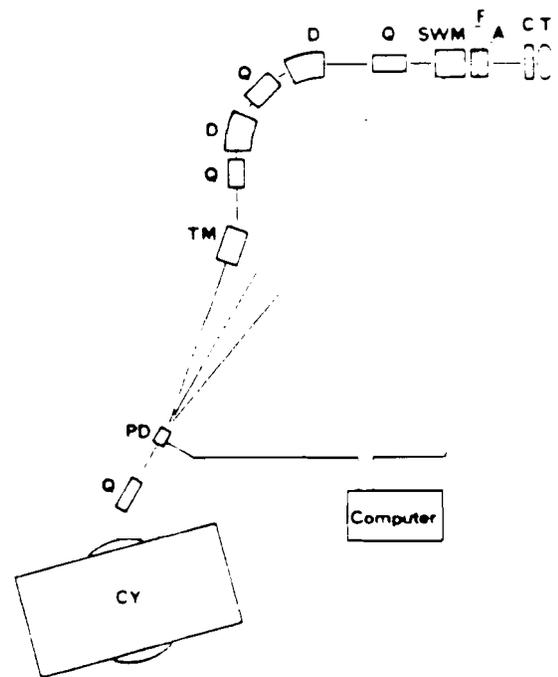
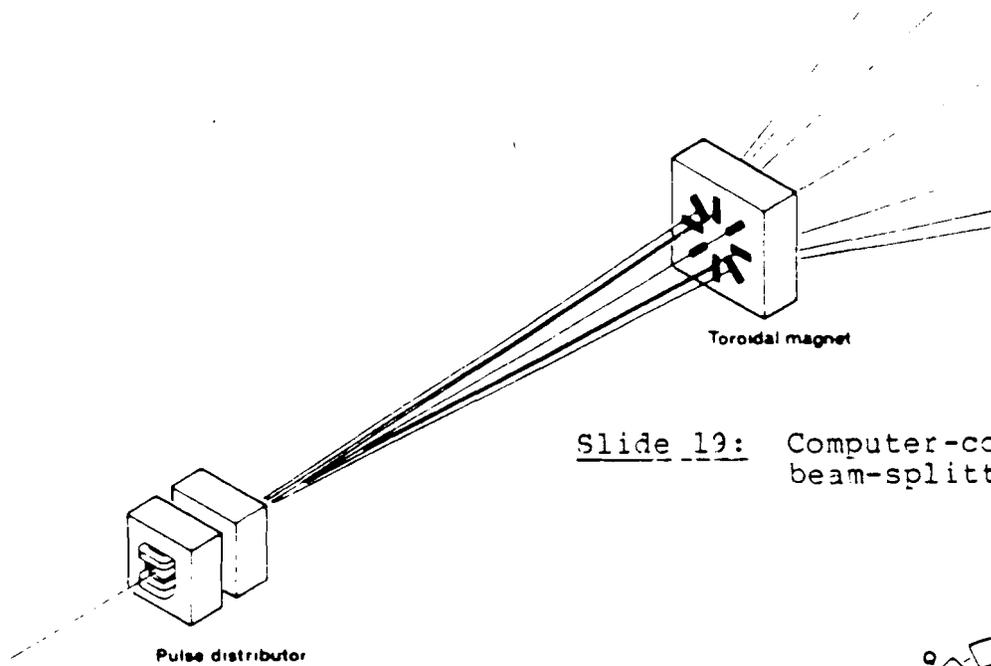


Slide 18: When the parameters X, Y, S and A (Slides 15 and 16) are afflicted by statistical spread ( $sX$ ,  $sY$ ,  $sS$  and  $sA$ ) the homogeneity will depend on the number of complete sweeps. The three curves shown were obtained for different sets of parameters;

Upper curve:  $G/S = 1.4$ ;  $sA = 0.5$ ;  $sS = 0.1$ ;  $sX = sY = 0.3$ .

Middle curve:  $G/S = 1.0$ ;  $sA = 0.5$ ;  $sS = 0.1$ ;  $sX = sY = 0.3$ .

Lower curve:  $G/S = 1.0$ ;  $sA = 0.198$ ;  $sS = 0.055$ ;  $sX = sY = 0.04$ .



Slide 20: Suggested beam transport system for an accelerator facility that would meet the demand specified in Slide 10b.

- CY cyclotron
- PD pulse distributor
- TM toroidal magnet
- Q quadrupole, triplet or doublet
- D bending magnet
- SWM sweeping magnet
- F filter
- T target (patient)
- C collimator
- A pulse current meter

Slides 19 and 20 are from S. Graffman, B. Jung and B. Larsson: Design Studies for a 200 MeV Proton Clinic for Radiotherapy, in "Proc. Sixth International Cyclotron Conference, Vancouver 1972", American Institute of Physics (1973).

Functional disorders of the brain, "radio-surgery"	25 (GWI) ; 2 (LBL) ; 12 (Gatchina)
Cancer of breast or prostate, irradiation of pituitary	250 (LBL) ; 50 (HCL) ; 60 (Gatchina) ; 174 (ITEP)
Diabetic retinopathy irradiation of pituitary	450 (HCL)
Pituitary adenomas	1,000 (LBL) ; 1.300 (HCL) ; 86 (Gatchina) ; 59 (ITEP)
Arterio-venous malformations in the brain	362 (HCL) ; 35 (Gatchina)
Small eye tumours (usually ocular melanomas)	300 (HCL) ; 45 (ITEP) 85 (LBL)
Malignant brain tumours	8 (GWI) ; 7 (HCL)
Cancer in the head and neck region	20 (GWI) ; 35 (HCL) ; 85 (LBL)
Cancer of oesophagus, lung or larynx	30 (Dubna)
Osseus sarcoma	27 (HCL) ; 17 (ITEP)
Cancer of anus or rectum	16 (HCL)
Cancer of the prostate	90 (HCL) ; 1 (ITEP)
Cancer of the uterus	110 (ITEP) ; 10 (GWI)
Cancer of the external genitals	89 (ITEP)

Slide 21: Clinical experiences with medium-energy proton beams. Data from Uppsala (GWI) and Dubna are not going to change before current rebuilding programmes have been completed. Data from Harvard (HCL) are from 1983. Data from Berkeley (LBL), Moscow (ITEP) and Gatchina are mostly from late 1981. Singular, exploratory studies have not been included.

From B. Larsson, J. Eur. Radiol. 5: 223 (1984).