PARTICLE THERAPY AT NAC: PHYSICAL ASPECTS

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The National Accelerator Centre (NAC) is the only particle therapy facility in the Southern Hemisphere and the only one in the world where both high energy neutrons and high energy protons are used for patient treatment. Routine treatment began on the p(66)/Be isocentric neutron therapy unit in 1989 and 764 patients had been treated in a variety of clinical protocols up to September 1995. The physical characteristics of the neutron beam are very similar to those of 8 MV x-rays. The present patient load of about 120 annually makes the NAC one of the few centres where significant numbers of patients are being treated with fast neutrons. Towards the end of 1993 the first patient was treated on the 200 MeV horizontal proton beam facility. A total of 98 patients had been treated up to September 1995. A unique patient positioning system based on stereophotogrammetric techniques has been successfully implemented and allows non-invasive and accurate patient set-up.

1. Introduction

The only hadron therapy facility in the Southern Hemisphere is at the National Accelerator Centre (NAC) at Faure, about 35 km from downtown Cape Town[1-4]. Routine treatment began in 1989 on the p(66)/Be neutron therapy unit (Elven Precision Ltd, Crawley, UK), while proton therapy was first undertaken in the NAC's 200 MeV beam in September 1993. It is the only facility in the world where both high-energy neutrons and high-energy (>150 MeV) protons are used for patient treatment. The NAC facilities were planned specifically to provide research opportunities in natural sciences for users from all over the country and other parts of the world, to supply high-energy particles for radiation therapy and to produce radioisotopes, primarily for medical applications.

All the major facilities, with the exception of the neutron therapy unit, were locally designed. The main accelerator is a variable-energy separated-sector cyclotron, capable of accelerating protons to a maximum energy of 200 MeV. The medical complex includes three radiotherapy treatment vaults, laboratories, offices, full medical physics and radiobiology facilities as well as a 30-bed on-site hospital. One of the treatment vaults contains the isocentric neutron therapy unit (66 MeV p/Be), while the 200 MeV horizontal beam proton therapy facility occupies a second vault. A second proton therapy beam line (possibly an isocentric unit) is foreseen for the third vault. Operating theatres are located close to this latter vault for use in possible future intra-operative proton therapy procedures. Neutron therapy patients are treated on Tuesdays, Wednesdays and Thursdays while proton therapy takes place at present on Mondays and Fridays. Future plans provide for 3 shifts per week each for both neutron and proton therapy.

All patients, including those from other parts of the country and from neighbouring territories, are referred to the NAC through one of the local university teaching hospitals, viz, Groote Schuur Hospital (University of Cape Town) or Tygerberg Hospital (University of Stellenbosch). Both hospitals are about 25 minutes by road from the NAC. At present all patient assessment and preparation as well as neutron treatment planning is undertaken at the teaching hospitals while proton treatment planning is undertaken at NAC. Although many patients are housed in the on-site hospital for the duration of their treatments, others attend as out-patients.

2. The neutron therapy facility

The p(66)/Be neutron therapy facility[3-8] incorporates an isocentric gantry capable of ± 185° rotation. A diagram of the gantry is shown in Figure 1. A rotating collimator (360°) with a continuously variable rectangular aperture provides field sizes between 5.5 cm^2 and 29 cm^2 at a source-to-axis distance (SAD) of 150 cm. A manually-controlled moving floor permits full rotation of the gantry. Downstream of the target are, in order, a pair of steel flattening filters (for small and large fields respectively), three tungsten wedge filters and a 2.5 cm thick polyethylene hardening filter, which removes unwanted low energy neutrons from the beam[9-11]. Blocks of 12 cm thick tungsten can be inserted in the beam downstream of the collimator for shielding purposes. Neutron dose rates are typically about 0.40-0.45 $Gy.min^{-1}$. A portal x-ray tube in the treatment head upstream of the collimator can be inserted on the beam axis and is used in conjunction with a neutron beam exposure for verification of the treatment field.

The physical characteristics of the NAC neutron beam are rather similar to those of an 8 MV x-ray beam as can be seen in Figure 2. The skin-sparing properties of the p(66)/Be beam are less pronounced than those of 8 MV x-rays as illustrated in Figure 3. This is due to the nature of the energy deposition processes of neutrons i.e. the

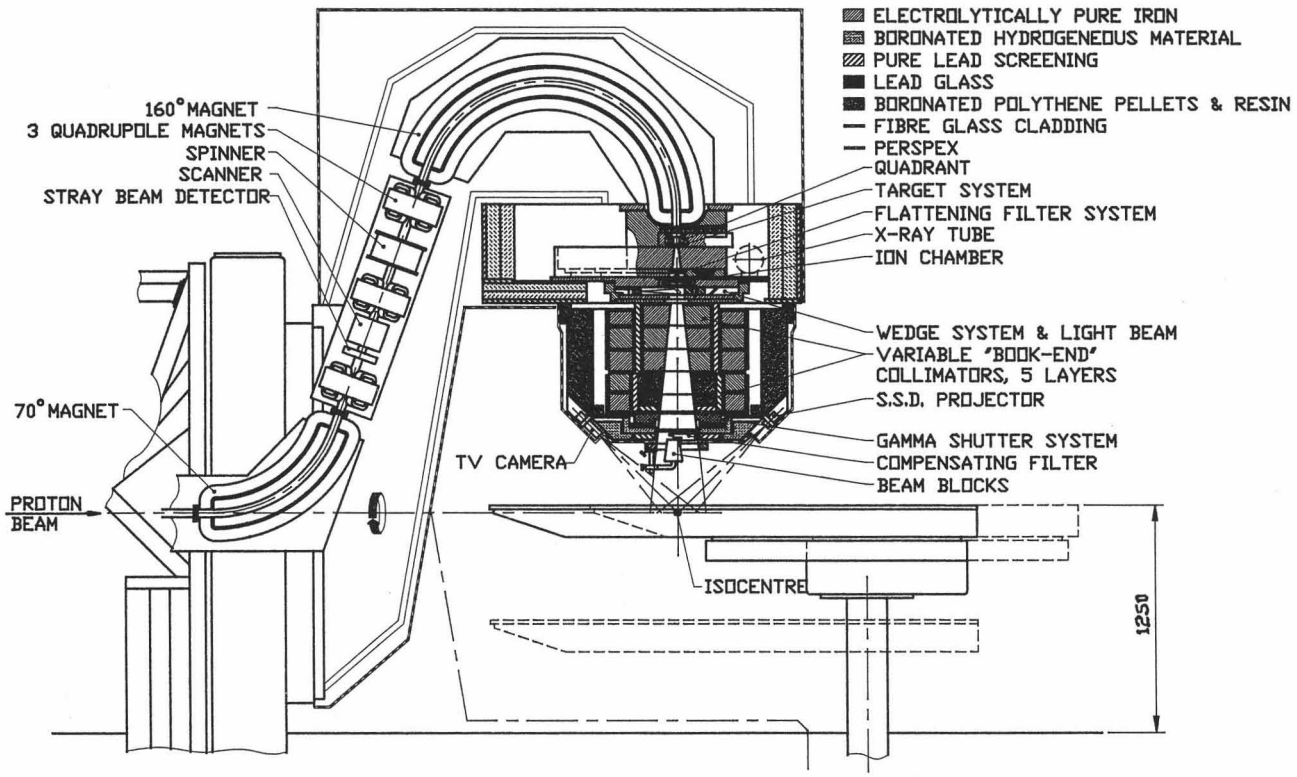

Figure 1: Diagram of the p(66)/Be isocentric neutron therapy gantry.

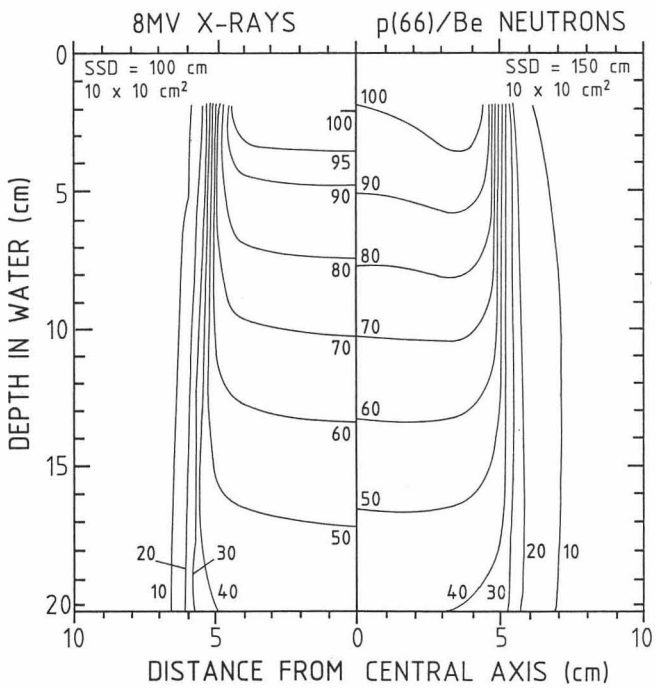

Figure 2: Isodose curves for the p(66)/Be neutron beam (right) compared with a typical 8 MV x-ray beam (left).

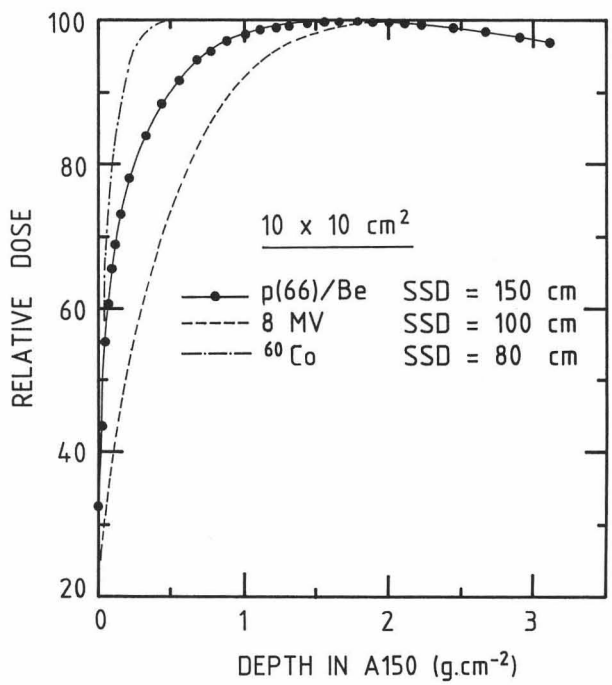

Figure 3: Build-up curves in the p(66)/Be neutron beam and in typical 8 MV x-ray and ^{60}Co beams.

production of short-range heavy recoils . If bolus materials are used, skin sparing can be restored by placing 1-2 mm of lead on the skin[13]. This removes most of the charged recoil particles. The gamma dose fraction on the beam central axis is a function of depth and field size and varies from about 3% to 12% of the total dose[14,15] as shown in Figure 4.

The energy spectra of the neutron beam for various irradiation conditions have been measured in air using the pulsed-beam time-of-flight technique[11] which is a unique capability in a clinical neutron therapy facility. Typical neutron spectra are shown in Figure 6.

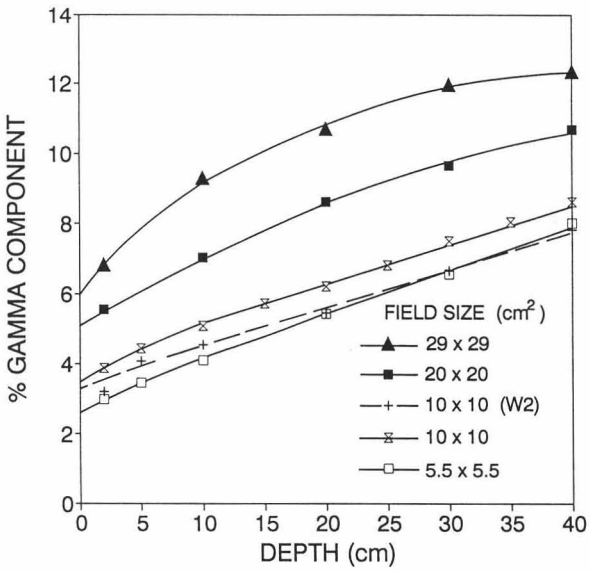

Figure 4: Central axis fractional gamma dose.

In order to verify the dosimetry and treatment prescriptions, international radiobiological[16] and national[17,18] and international[19-21] dosimetry intercomparisons have been undertaken. The results obtained were highly satisfactory, showing good agreement between participating centres. Several other radiobiological measurements have been made[10,22-27] and the RBE and OER of the NAC's neutron therapy beam have been found to be similar to those measured at other high energy p/Be neutron therapy facilities[23]. Several microdosimetry[10, 28-30] (Figure 5) and other beam characterisation experiments[31, 32] have been completed. The energy spectra of the neutron beam for various irradiation conditions have been measured in air

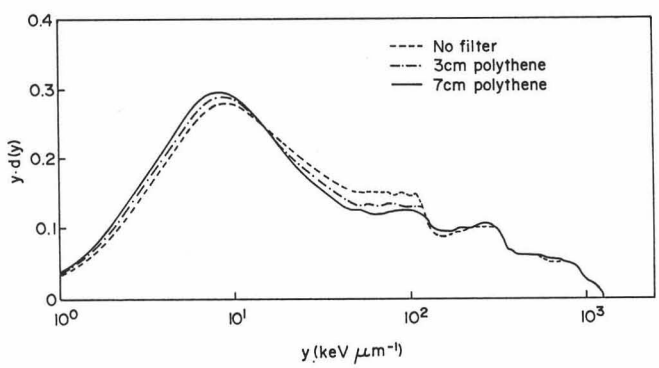

Figure 5: Microdose spectra for different filters[10].

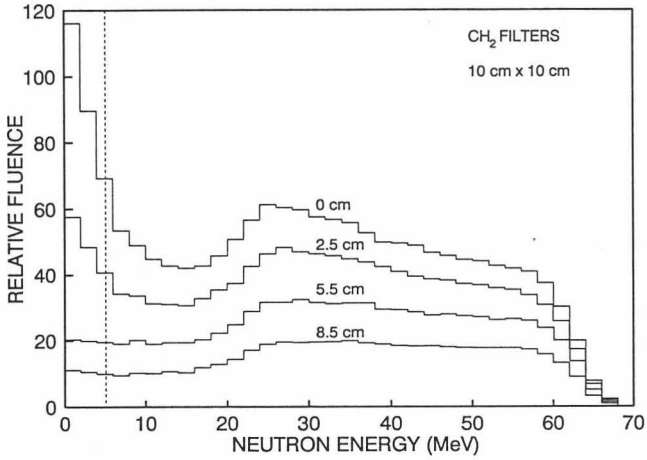

Figure 6: Neutron spectra for different filters.

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Several randomised clinical trials[33] are currently being undertaken at NAC, including treatments of tumours of the head and neck, salivary gland and breast and treatments of soft tissue sarcomas, uterine sarcomas, paranasal sinuses and mesotheliomas (Table 1). A protocol for prostate treatments is presently being formulated. A significant number of non-trial patients are also being treated (Table 1). A typical plan for the neutron treatment of a pelvic tumour is shown in Figure 7. Also shown on the figure is the treatment plan for 8 MV x-rays for the same tumour. These two plans emphasize the similarity in dose distributions of the two types of radiation.

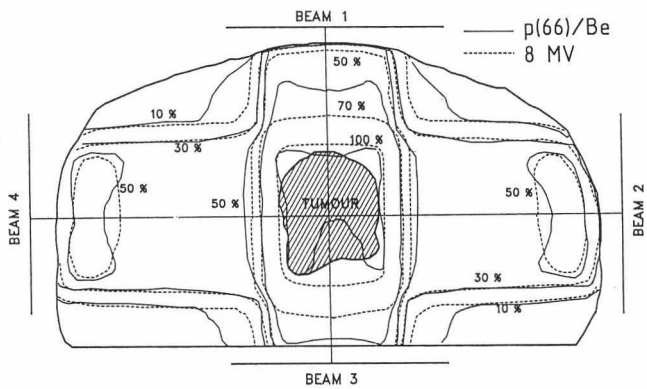

Figure 7: Comparative treatment plans for a pelvic tumour.

Up to September 1995 a total of 723 patients (20875 treatment fields) had been treated on the neutron therapy facility. The 110-130 patients treated annually constitute a significant proportion of the current world-wide patient load. At present most patients are given 3 weekly fractions for 4 weeks. The facility has operated very reliably with 96% of the scheduled treatments having been successfully completed to date. The average treatment time per field (including patient set-up) is 12 minutes and the average number of fields per fraction is 2.6.

TABLE 1: NEUTRON THERAPY TREATMENTS

SITE	NUMBER OF PATIENTS	
	TRIAL	NON-TRIAL
Head and neck	141*	71
Salivary gland	192	
Soft tissue sarcoma	64	
Breast	74	14
Uterine cervix†	5	
Bronchus†	6	
Uterine sarcoma	45	
Mesothelioma	21	
Paranasal sinus	26	
Bone tumour		62
Malignant melanoma		25
Sundry		18
	574	190

**Includes patients treated in photon arm*
†Discontinued

3. The proton therapy facility

The horizontal 200 MeV proton therapy facility for irradiations of intracranial and head and neck lesions was commissioned in September 1993[5, 34]. A schematic layout of the beam delivery system is shown in Figure 8. The total distance between the vacuum window and the isocentre is 7 m. A double scatterer plus occluding ring system[35] is used to flatten the proton beam. The beam delivery system is designed for a maximum field diameter of 10 cm. Figure 9 shows typical isodose curves for an unmodulated 10 cm diameter beam with a residual range of 24.5 cm in water.

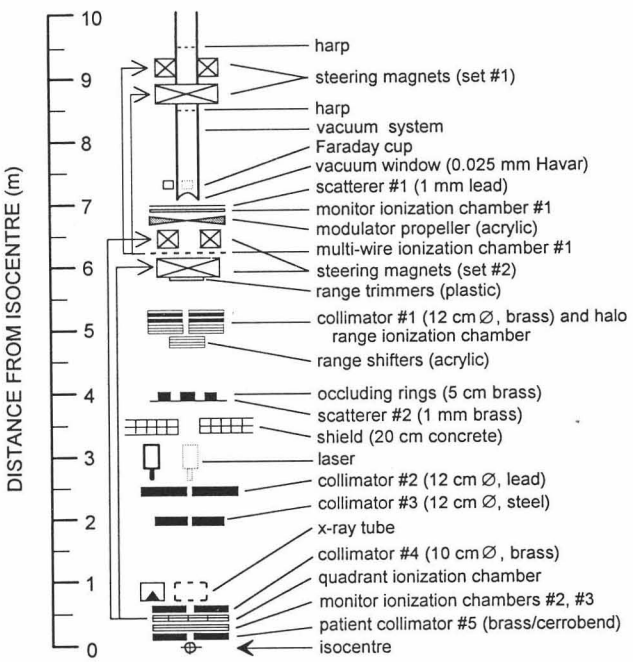

Figure 8: Schematic diagram of the 200 MeV horizontal proton therapy facility.

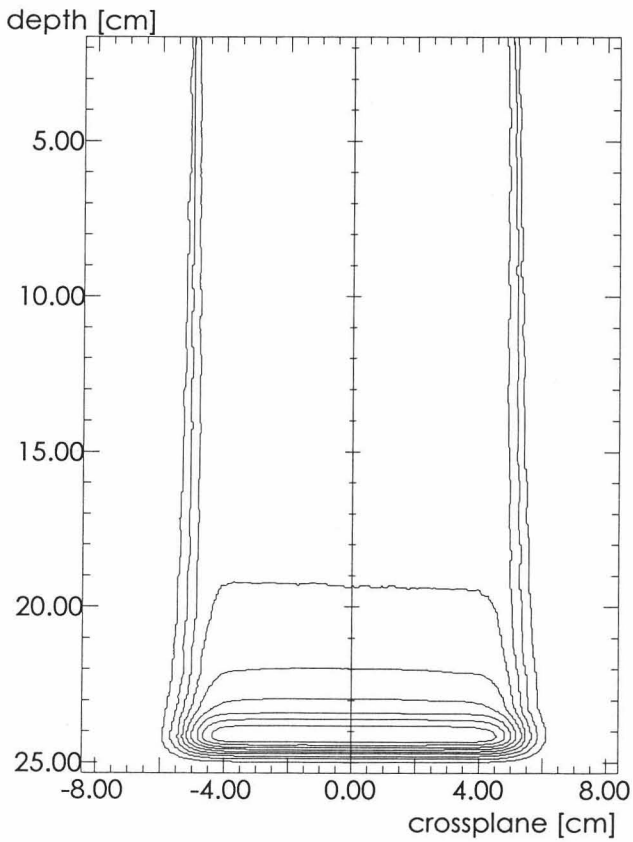

Figure 9: Isodose (10%-90%) distributions for an unmodulated proton beam.

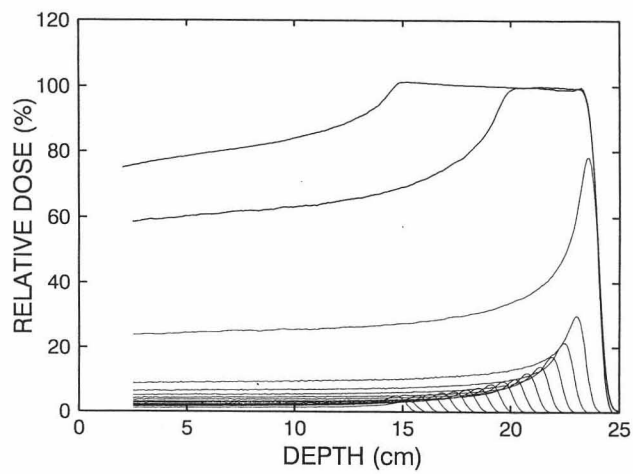

Figure 10: Range-modulated proton depth dose curves. The weightings of the range-shifted individual curves which are used to design the modulator propeller are also shown.

The Bragg peak is spread out longitudinally using propellers made up of different thicknesses of acrylic and which are rotated in the proton beam[36] as shown in Figure 10. Since the beam energy cannot be reproduced exactly every day plastic range trimmer plates, 0.6 mg.cm^{-2} thick are placed just upstream of the modulator propeller (Figure 8) in order to routinely produce a residual range of 24.00 ± 0.03 cm in water (distal 50% level) for patient treatment. This range corresponds to a proton energy of 191 MeV. For spread-out Bragg peak (SOBP) therapy additional acrylic degraders are inserted in the beam to achieve the required range.

The beam is controlled by two computerised feedback systems acting on two sets of XY steering magnets. The first system uses information from the multiwire ionization chamber, while the second one uses the information from the quadrant ionization chamber (Lawrence Berkeley Laboratory, California) immediately upstream of the final collimator. The final (patient) collimator (#5) is located 27.5 cm upstream of the isocentre. Fixed inserts, which are usually custom-made of cerrobend, fit into the final collimator assembly which can rotate around the beam axis for alignment with the required treatment field. Clinical dose rates of about 3 Gy.min^{-1} are routinely used. Individual calibrations are performed for each treatment field.

Several microdosimetric[37] (Figure 11) and radiobiological[38,39] measurements have been made in both monoenergetic and modulated 200 MeV proton beams. A RBE of 1.00 was measured in the plateaux of both monoenergetic and modulated beams while RBEs of 1.07 and 1.16 were obtained in the middle and at the distal edge respectively of a 10 cm spread-out Bragg peak[39]. Proton dosimetry[40-42] and radiobiological[43] intercomparisons have also been undertaken with various overseas centres and the results obtained were highly satisfactory. Proton spectra have been measured in the clinical beam under a variety of conditions using proton elastic scattering techniques. A feature of the spectra is the very small low-energy component in the beam as shown in Figure 12.

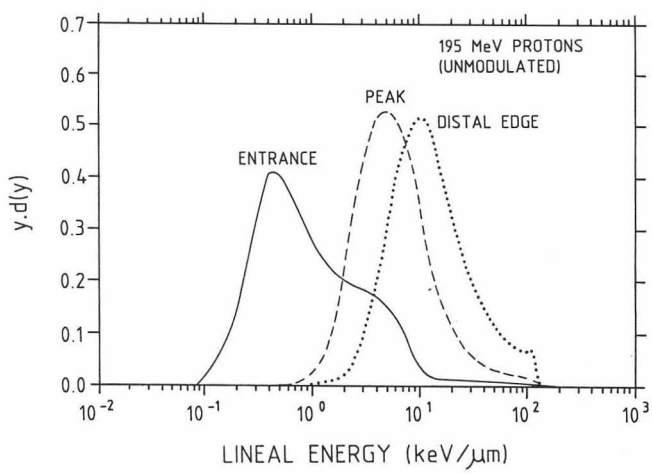

Figure 11: Microdose spectra at different positions on the Bragg curve.

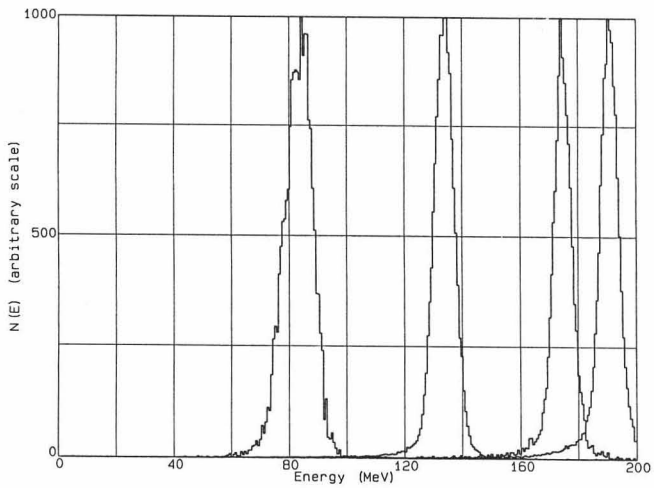

Figure 12: Proton spectra for full-energy (right hand side spectrum) and degraded beams.

The unique patient support and positioning system[44-47] used at the NAC was designed by the Departments of Mechanical Engineering and of Surveying and Geodetic Engineering of the University of Cape Town in conjuction with the Division of Medical Radiation of the NAC. The system makes use of real-time digital stereophotogrammetry (SPG) techniques, which are commonly used in land surveying, and is linked to the patient support system which is a computerised adjustable chair with 5 degrees of freedom. When a patient undergoes a CT scan to locate the treatment volume, small radiopaque targets (1 mm diameter) are affixed to a custom-made plastic mask which fits the patient's head precisely. From the scan information three-dimensional coordinates for all the targets are determined relative to a reference point in the treatment volume. This reference point is normally taken as the treatment isocentre. Retroreflective markers 8 mm in diameter are then fixed accurately on the mask exactly over the radiopaque markers. A close-fitting back is made for each patient mask and is fitted with a device for fixing the patient to the fully-adjustable chair headrest. In order to compensate for the chair's lack of a roll motion the patient's head often has to be tilted slightly from the vertical to allow positioning to be accomplished more efficiently.

During the patient positioning stage, a set of three charge-coupled device (CCD) TV cameras (out of eight which are positioned around the isocentre) captures video images through a frame-grabber of the retroreflective markers on the patient mask. These images are then analysed by a personal computer using SPG techniques. Since the positions of the video cameras and the direction of the proton beam are accurately known in space, it is possible to calculate the position of the centre of each of these reflective markers and hence the position of the reference point in the treatment volume, relative to the beam axis. The effects of camera distortions, aspect ratio and perspective are taken into account in the calculations. The coordinates of the beam entry point are also required and are obtained from the treatment planning programme.

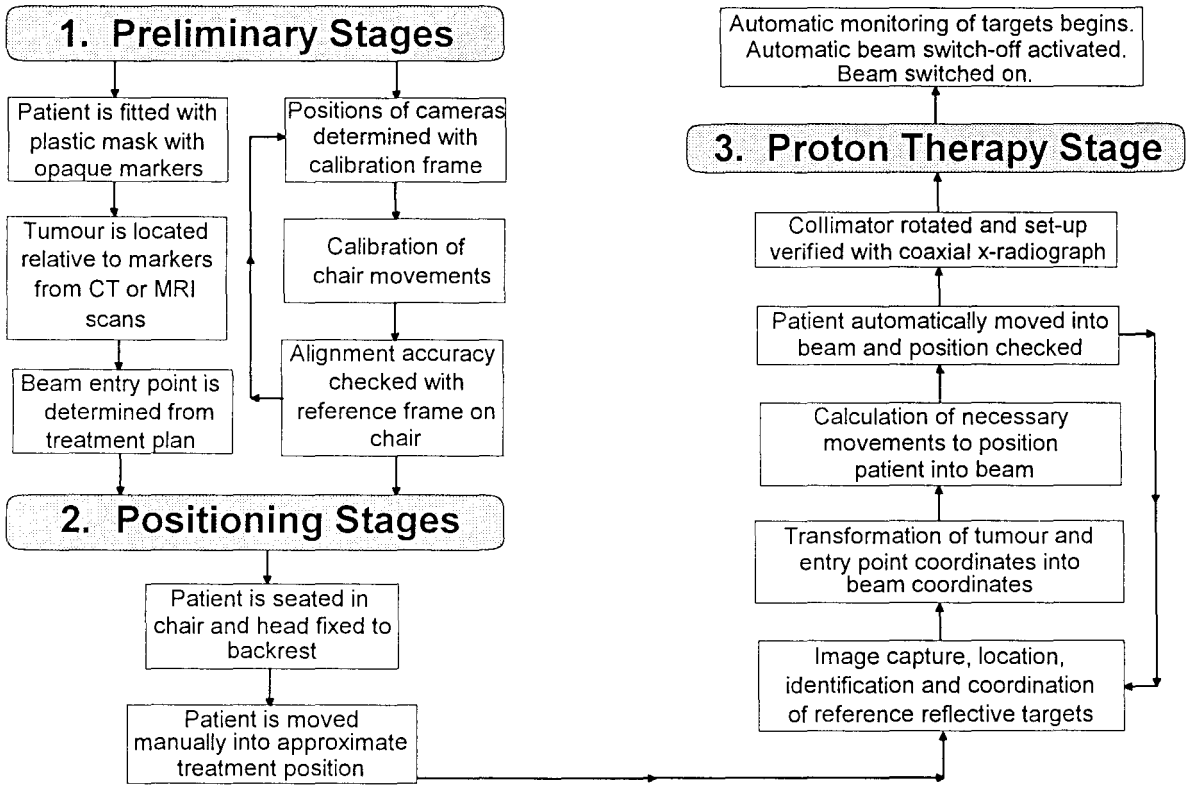

Figure 13: Block diagram of the procedures involved in patient preparation, positioning and treatment.

Spatial corrections to align the vector between the beam entry point and the reference point (isocentre), which is in the treatment volume, with the beam axis are then sent from the SPG computer to a second personal computer which controls the patient support system (chair). Computer-controlled stepper motors move the chair by the required amounts (X,Y and Z translation accuracy is within 0.1 mm and within 0.1 degree for seat and vertical rotations) to bring the treatment vector directly into the proton beam. Additional information regarding the rotation angle of the final patient collimator, to align the collimator with the outline of the treatment volume, is also calculated by the first computer. It takes typically 2-3 iterations from an arbitrary position to align the patient in the required orientation.

Once the patient is properly positioned, according to preset tolerances of the beam entry, tumour and reference points (normally ±0.5 mm), the system is then set to monitor the positions of all the reflective targets and hence the position of the treatment volume. The beam can then be switched on and will be switched off automatically if any of these targets move by more than a preset amount. Including patient set-up, positioning, checking of position (with theodolites or lasers), x-ray verification procedures and irradiation the average total time to treat a field is 25 minutes. Analysis of the portal radiographs shows that the positioning accuracy of the SPG system is better than 1 mm (1 standard deviation).

A block diagram of the procedures invloved in patient preparation, positioning and treatment is given in Figure 13.

A sophisticated 3-dimensional non-coplanar treatment planning system (PROXELPLAN) is used for planning proton treatments at NAC. The system is based on VOXELPLAN, obtained from the German Cancer Research Centre, Heidelberg and a proton therapy module developed at the Royal Marsden Hospital, London. The latter module has been extensively modified to make the hybrid planning system suitable for clincal use. For most treatments spread-out Bragg peaks are used but for smaller lesions (≤20 mm diameter) crossfire plateau irradiations are given. Most treatments have been stereotactic radiosurgical procedures given in 3-4 fractions. Such fractionated treatments are possible because of the non-invasive nature of the patient immobilization and positioning system. Isodose curves in the transverse and sagittal planes for a typical non-coplanar treatment plan of an intracranial lesion are shown in Figure 14.

Up to September 1995 a total of 98 patients (897 fields) had been treated for a variety of conditions, most commonly brain metastases, ateriovenous malformations, meningiomas, gliomas, acoustic neuromas and pituitary adenomas (Table 3). The average number of fields per fraction is 3.2 and the average number of fractions per treatment is 3.1.

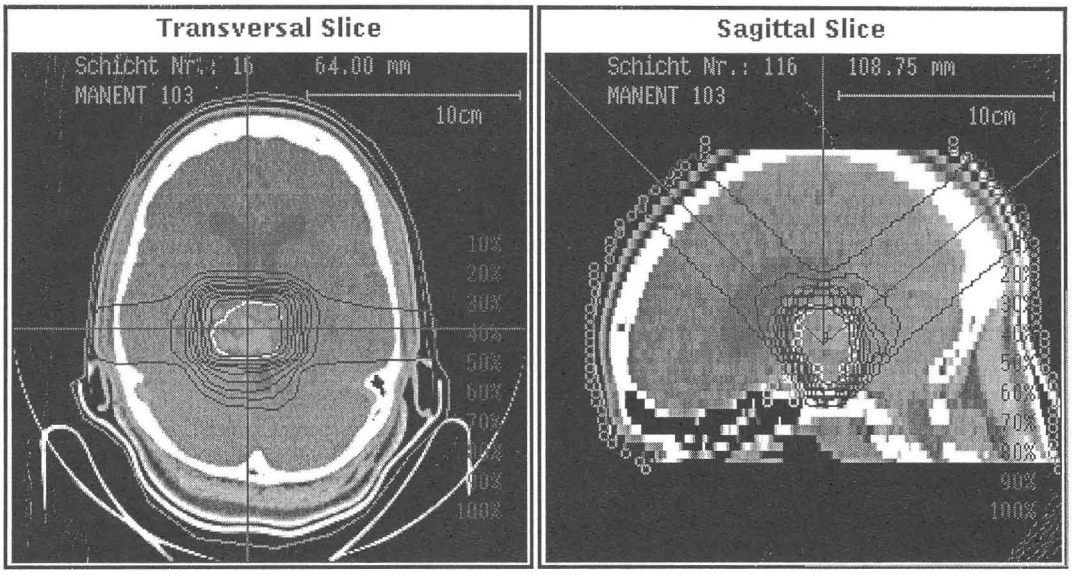

Figure 14: Typical plan for a 4-field non-coplanar treatment of an intracranial lesion.

TABLE 3: PROTON THERAPY TREATMENTS

DIAGNOSIS	NUMBER OF PATIENTS
AVM	23
Meningioma	15
Brain metastasis	14
Pituitary adenoma	12
Acoustic neuroma	12
Low grade glioma	4
High grade glioma	2
Paraspinal metastasis	2
Skull-base carcinoma	2
Craniopharyngioma	2
Sundry	10
	98

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