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POSSIBILITIES OF USING THE NAL LINAC FOR CANCER THERAPY

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I. Introduction

A renewed interest in the use of heavily ionizing particles for radiation therapy has developed in the last few years. This is a reflection of the need for more effective treatment of some malignant tumors than that achieved solely with the conventional x rays and electrons. More attention is being given to beams of negative pi-mesons with their star production at an appropriate depth in tissue, to sources of neutrons with their attendant knock-on protons and other heavy ions, to beams of protons with their pronounced Bragg peak of energy loss at a depth in tissue, and to beams of still heavier ions.

Wilson[1] pointed out the possible use of fast protons for radiation therapy in 1946. Some experimental and clinical work with protons and heavier ions followed. Publications include, as a partial list, reports on work done at Berkeley,[2,3,4] Uppsala,[5-8] Harvard,[9,10,11] and Dubna.[12]

There are several advantages that protons have over commonly used radiations. The Bragg peak near the end of the proton's range means, of course, that the dose in a tumor can be much higher than in the healthy tissue near the skin. The peak is too narrow for most tumors but it can be transformed into a plateau of appreciable width by using a range of proton energies. This energy spread can be achieved by use of variable absorbers in the beam or by variation of the primary proton energy. An example of such a transformation is shown in Fig. 1, taken from a paper by Larsson.[13] By contrast, the dose distribution of x-rays and neutrons is nearly exponential. Electrons show no Bragg peak because of effects of much multiple scattering and bremsstrahlung.

Because the density of ionization is higher in the Bragg peak than elsewhere, the radiobiological effectiveness (RBE), which increases with ion density, is higher in the peak, further increasing the effect of the higher physical dose.

Tumors are known to outgrow their vascular supply, thereby producing some anoxic cells, which are more resistant to x-radiation than are oxygenated cells. It may be that these anoxic cells are less resistive to the more heavily ionizing protons.

Finally, protons produce dose patterns with more sharply defined boundaries, both laterally and at the terminus than do most other radiations under consideration.

The range of 200-MeV protons (~ 25cm) from the NAL linac is sufficient to treat deep-lying tumors. Most energies up to 200-MeV can be reached automatically in rapid succession by controlling the linac through computer programming. Alternatively or in combination with linac control, variable absorber thickness can be used to give a range of energy. Normal operating beam intensity from the linac is far in excess of requirements for therapy and must be reduced by computer control and by collimators.

Use of the linac beam for medical purposes during that part of each main accelerator cycle not requiring beam would be straightforward. The linac operates at 15 pulses per second. It delivers 12 consecutive pulses to the booster and thus to the main ring. During the remainder of a 2-5 second main accelerator cycle, the linac beam can be directed into a separate beam line and treatment facility. The two modes of operation would be compatible with no restrictions placed on the primary accelerator operation.

The proper evaluation of proton therapy as a successful technique would be aided by the advantages inherent in the Chicago area location. There are several medical schools and hospitals in Chicago with existing radiotherapy centers. Several radiotherapists from a number of institutions have already expressed an interest in the potential of a treatment facility at NAL. A large number of patients would have access to NAL following the preliminary research. Under the proper direction, the statistical analysis of the treatment program could therefore become meaningful.

II. Present Linac Description

Design details and initial performance data for the linac have appeared in several reports.[14-17] A simplified layout of the machine installation is shown in Fig. 2. There are nine cavities coming after a short 750-keV transport line from the preaccelerator. Each cavity is energized by a radio-frequency power amplifier located in an equipment bay adjacent to the linac tunnel.

The basic linac design permits acceleration of beam currents to 100 mA in pulses up to 100 μsec in length and at a repetition rate of 15 pps. A beam of 100 mA has been accelerated to 200 MeV. Most of the operation thus far, however, has been at much lower currents in the range of 15-30 mA, and at much shorter pulse lengths during the tuneup phase of the linac, booster, and main ring accelerators. Most of the studies on the linac beam properties have been made also in this current range.

The beam diagnostic equipment includes several beam current toroids in the 750-keV and 200-MeV beam transport lines as well as toroids at the entrance and exit of each linac cavity. An example of beam-current display from these toroids along the length of the linac is shown in Fig. 3. (The buncher cavity in the 750-keV line, which doubles the accelerated current, was turned off for these data). The emittance of the beam in both transverse planes can be measured, in several seconds time, destructively at 750 keV and 10 MeV and nondestructively at 200 MeV. An example of a beam emittance display at 200 MeV obtained from wire-scan beam profiles is shown in Fig. 4. The output energy of the linac beam and its energy spread are determined by a wire scan at the output of a spectrometer magnet. Figure 5 shows a total momentum spread of approximately 0.2%. The relative phases of the 200-MeV rf fields in all the linac cavities are important in determining the output energy and energy spread. In general operation, the practice has been to adjust the phases of cavities 8 and 9 to set precisely the output energy and energy spread.

The values of beam emittance and momentum spread indicated here are perhaps better than needed for transport through a medical physics beam line, but the good stability and reproducibility of these values achieved from pulse to pulse and hour to hour is important.

Control and monitoring of the linac have relied on a computer-based control system[18-20] which is able to produce plots like those in Figs. 3-5. Numerous other displays are used during tuneup and operation. This system has included a computer-controlled beam-pulse inhibit when the gradients or field levels in the accelerating cavities are outside of a prescribed operating range. In such a situation, the beam pulse of the preaccelerator is shifted out of time coincidence with the radio-frequency fields in the linac cavities. On the other hand, an auto gradient mode is frequently chosen whereby the computer automatically sets the gradients back to their prescribed values.

At the high-energy end of the linac, two beam dumps are shown: one for the straight beam line and one for the momentum analysis line, A "chopper" followed by a septum magnet placed near the end of the linac enables a short piece of beam pulse to be directed into the booster injection line. Details of the 200-MeV transport area have been reported elsewhere.[21] See Fig. 6.

Projected operation of the linac-booster injection system requires injection of 12 consecutive pulses at 15 pps into the main ring at the beginning of each main ring cycle of 2 or more seconds. Each linac pulse is long enough to permit at least an 11-μsec portion to fill the booster with four turns or more of 65-mA beam so that 5×10^{13} protons are delivered to the main ring on each cycle. Any beam produced during the remainder of a main-ring cycle by the injector would be for diagnostic purposes only. The length of a main-ring cycle depends on a combination of final energy, and therfore the length of magnet ramp, and the desired length of beam spill.

III. Flexibility of Linac Operation and Beam Handling

The capability for variation of linac energy and beam current is of prime interest when one considers use of the linac beam for medical purposes. Energies in the range of 50 to 140 MeV might be needed frequently. Also, exceedingly small currents are required on a patient. Table I shows the energies out of each of the nine accelerating cavities. By inhibiting the rf excitation in one or more of the cavities beginning at the high energy end, one can transport lower energy beams to the end of the linac. Experience has shown that such lower energy beams are transported well through the linac with no necessary changes in the magnetic focusing system of the linac, except for the lowest energies available. Some adjustments to the last few quadrupole magnets of cavity nine and to the magnets in the 200-MeV transport line are required to get reasonable transport of the lower energy beams to the dumps.

Variation of the energy by phase changes in the last of a series of cavities is shown in Fig. 7 from some theoretical calculations made at BNL.[22] Such variation has been verified roughly on the NAL linac. A continuous range of energies could then be made available by programming the phase of the last appropriate cavity and by use of absorbers to fill gaps in the energy range not reached by such phasing. Further study may well indicate that all energies of interest are possible without absorbers by more complicated phasing schemes than the one indicated by the preceding curves. Alternatively, variable absorber thickness could be used to provide all energies by degrading a beam of fixed linac energy.

One has, through the flexibility of computer control, however, the means to eliminate or minimize the scattering and neutron production present in the absorber technique.

The need for reduction of beam intensity from normal booster injection levels can be illustrated by an example. Suppose one required a single daily dose of 4×10^{-7} coulombs of charge in the proton beam. This approximate number can be obtained by requiring 250 rads at a transformed Bragg peak in the tumor area and assuming up to 200 rads at the skin for a large, 35cm x 35cm, field.[23] Suppose further that this dose will be delivered in 3000 10-μsec-long pulses at 15 pps for two seconds of each three-second main ring cycle. The time required is five minutes. For a linac beam current I and collimation reduction factor f, the pulse current arriving on the field is

$$If = \frac{4 \times 10^{-7} C}{3000 \cdot 10 \mu sec} = 13 \mu A$$

If the collimation factor were 10^{-2}, the linac beam would be 1.3 mA.

There are many ways to reduce the beam intensity. One obvious way is to inhibit the buncher. Another is to reduce the pulse length. If done at the ion source, the practical lower limit at present is about 3 μsec. Fast acting slits in the 750-keV line, though possible, are probably less desirable than electronic variation of the ion source parameters. Reduction of arc current and/or magnet current in the source, when done in a way not to effect normal accelerator operation, is a very effective way to reduce beam to the one-mA level. Other computer controlled methods include reduction of the first linac cavity gradient or the preaccelerator voltage to just above threshold for acceleration. Later collimation after the linac, at the final energy desired, can provide the final reduction in intensity needed as well as give the required beam size and uniformity for easy handling.

A number of methods for extracting beam into a medical physics transport line appear feasible: a) Taking beam directly through the existing momentum beam dump. This may require delivery of the same energy beam always or replacement of the present momentum spectrometer magnet with a faster, pulsed magnet. b) Taking beam from one of the existing beam lines by the kicker plus septum magnet method now in use for the booster line. Space is at a premium. d) Extraction between cavities 8 and 9 by a pulsed magnet to kick the beam through a hole in the side of cavity nine. This has the desirable feature of leaving the present 200-MeV area intact. The maximum energy would be reduced by 20 MeV, however.

Use of linac beam for medical purposes during only the time when the booster does not need beam is suggested. Linac energy is then easily adjustable. It may be worth noting in addition that time sharing with the booster of the same linac beam pulse at a fixed energy is possible and completely compatible with the primary purpose of the linac. Means of varying the beam intensity as well as energy in the proton therapy line would, of course, be more limited in this mode of operation.

A Design Example

In the following we give one set of ideas appropriate to a particular way of providing linac beam to the target or the treatment room. The ideas are conceptual and represent no engineering design at this point beyond our existing linac facilities. Flexibility of computer control is used to vary beam energy and intensity within the linac itself in this approach. It could turn out, after more study, that this method offers no important advantages over strictly absorber and collimation methods of controlling energy and intensity within the extracted beam line alone. Some consideration is given in what follows also to minimizing beam-handling magnet sizes. If magnet aperture were of little concern, one might do things differently, particularly in preparing the beam for the treatment room.

Between linac cavities 8 and 9, there is a space of approximately 65 cm length which could be occupied by a small pulsed bending magnet. Energizing this to a field of 8 kG, during the time when the booster does not need beam, enables the beam to clear the 16 cm diameter drift tube at the input of cavity 9 and come through the side wall of this cavity. Bending and focusing quadrupole magnets, of programmable type for various energies, could then carry the beam through a transport line to the medical area. See Fig. 8 for a rough schematic of the beam line, showing expansion to multiple treatment rooms if desired.

It is assumed that the beam will be reduced to the order of one mA in the linac for this operation. The emittance area of such a low-current beam, based on measurements at 15 mA, should not be more than a few tenths of a mrad-cm. It should be very easy to transport. This reduction in beam current from the typical 50 to 100 mA level can be achieved by reducing the values of the arc current and magnet current in the ion source.

The beam energy can be programmed over a large range downward from 181 MeV by changing intercavity phases of the rf fields and by shifting the rf field pulse in the higher energy cavities V off time relative to the ion source pulse. Absorbers can be added in the extracted beam line, if needed, to fill gaps in the energy spectrum.

Selection of the best method for delivery of beam to the target so that the field is covered uniformly to within ± 2 or 3% and with sharp boundaries requires some study. A scanning method using a small beam spot is possible. For the larger field areas, however, it would appear that, for a 15 pps repetition rate, the time required to scan in three dimensions, laterally and in energy, would be too long for patient comfort. Use of a ridge filter to spread the energy helps, but the scan time is still quite long. This problem is solved if one has sufficient reliability of equipment to rely on uses of only a few beam pulses of relatively high beam current at each spot. We are assuming, however, that for safety we wish to integrate at least 50 pulses to reach the design dose at each spot. At the proper level, the computer will stop the beam and move it to the next location.

It is of interest to investigate the possibility of covering the whole target field, or a significant portion of it, with each beam pulse. One can spread a beam with quadrupole magnets plus a drift space so that a large area like 35 cm x 35 cm can be covered. The usual beam, however, is not of uniform density across its width, but more frequently nearly guassian. Because of the need for severe collimation to reduce beam intensity anyway, one can spread the beam and then select only the center by collimation to obtain an approximately uniform beam.

For example, assume a 1.3mA beam with an emittance area of .5 mrad cm. Form a circular parallel beam of 5 cm diameter. The maximum angle of divergence is

$$\alpha = \frac{0.5 \times 10^{-3}}{2.5\pi} = 0.06 \times 10^{-3} \text{ rad.}$$

With sets of slits, now collimate to a square beam of 0.4 cm keeping ~1% of the beam. This is now a uniform beam, quite parallel, which can be spread by one or two small bore quadrupole magnets plus a drift space to yield a large area uniform beam. Care must be used in alignment to avoid undesirable steering.

In Fig. 9 the 90° bend magnet is 3.5 meters above the target. It is another 3.5 meters approximately back to the last quadrupoles. If each quad is 50-cm long, a field at the edge of the beam of 1 kG (or a gradient of 5 kG/cm) will spread the beam to a width of 35 cm on the target. If the 90° bending magnet has a large aperture in the horizontal direction, the whole target can be irradiated on each pulse. By using an average of 50 pulses at each proton energy and 60 energy steps, 5 minutes of irradiation are required giving a total dose of 4×10^{-7} coulombs. Alternatively, the beam can be kept narrow in one dimension and scanning done in this dimension with one of the dipoles shown in the figure. Large fields now require much more time. If an irregularly shaped field is required, this can be obtained by scanning with one dipole in the narrow beam direction and programming both the quadrupole strength and the other dipole appropriately. A pattern collimator could be used in front of the target as a safety limit or as an alternate way of shaping the field.

The whole linac plus beam handling system as described here appears quite complex with much computer control of many elements required. From experience, computer control is feasible and would be used for some mode of operation. There are other less complicated modes which can be used and further study of the dose accuracy and reliability must be made to determine which mode is preferred.

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Table I

Cavity Number	Output Energy (MeV)
1	10.42
2	37.54
3	66.18
4	92.60
5	116.5
6	139.0
7	160.5
8	181.0
9	200.3

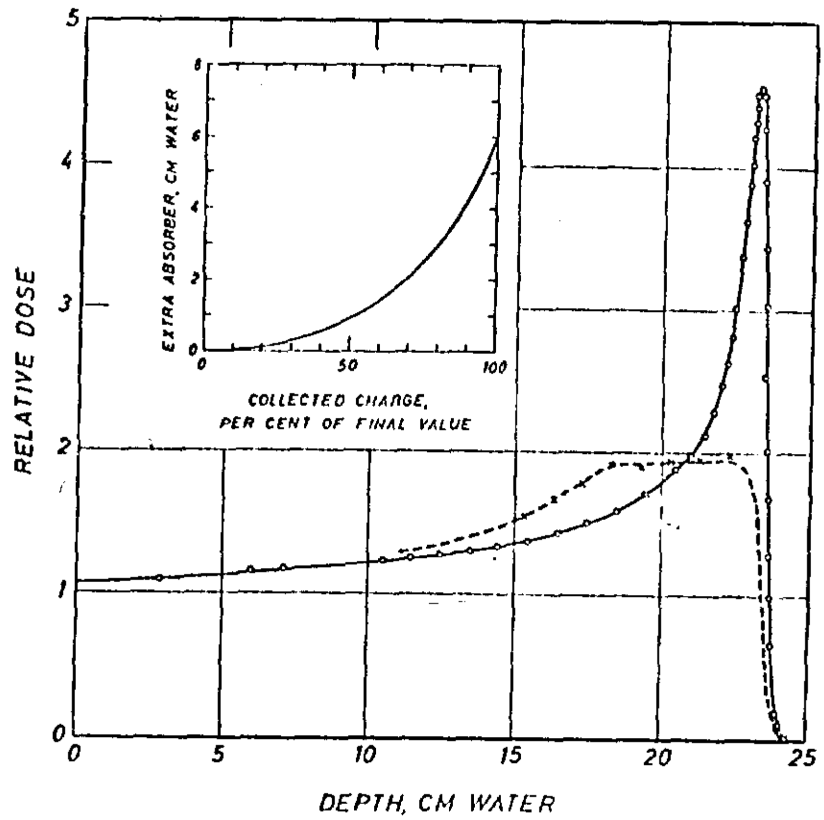

Fig. 1. Example of transformation of the Bragg peak. Variation of the thickness of the absorber was performed according to the curve in the inset diagram. The large diagram shows the original (——) and the calculated transformed (-----) depth-dose curves. The crosses give the results of measurement of points on a depth-dose curve obtained by use of a ridge filter of the type described in the text. The profile of the ridges was determined by the shape of the curve in the inset diagram, one cm water being equivalent to 0.18 cm brass.

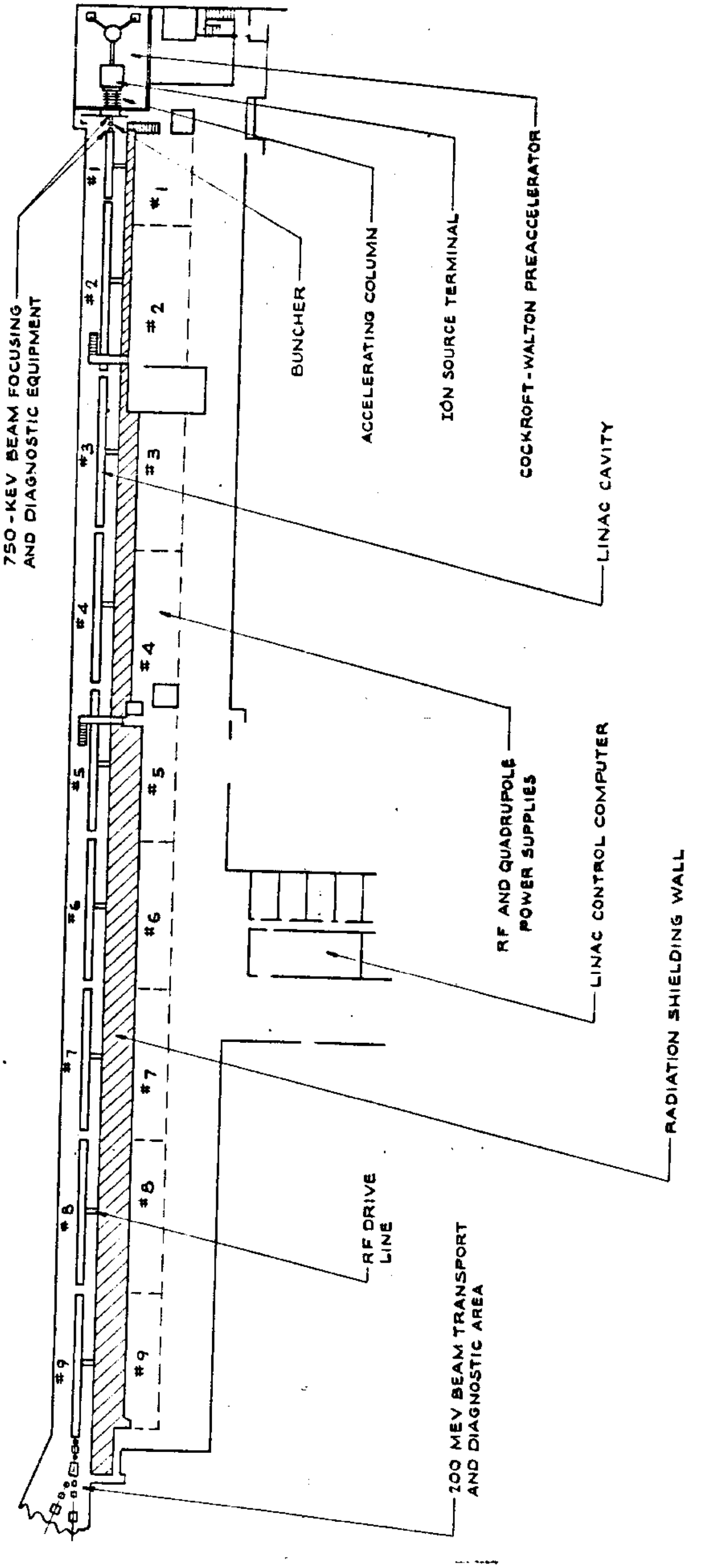

Fig. 2. Simplified plan view of linac.

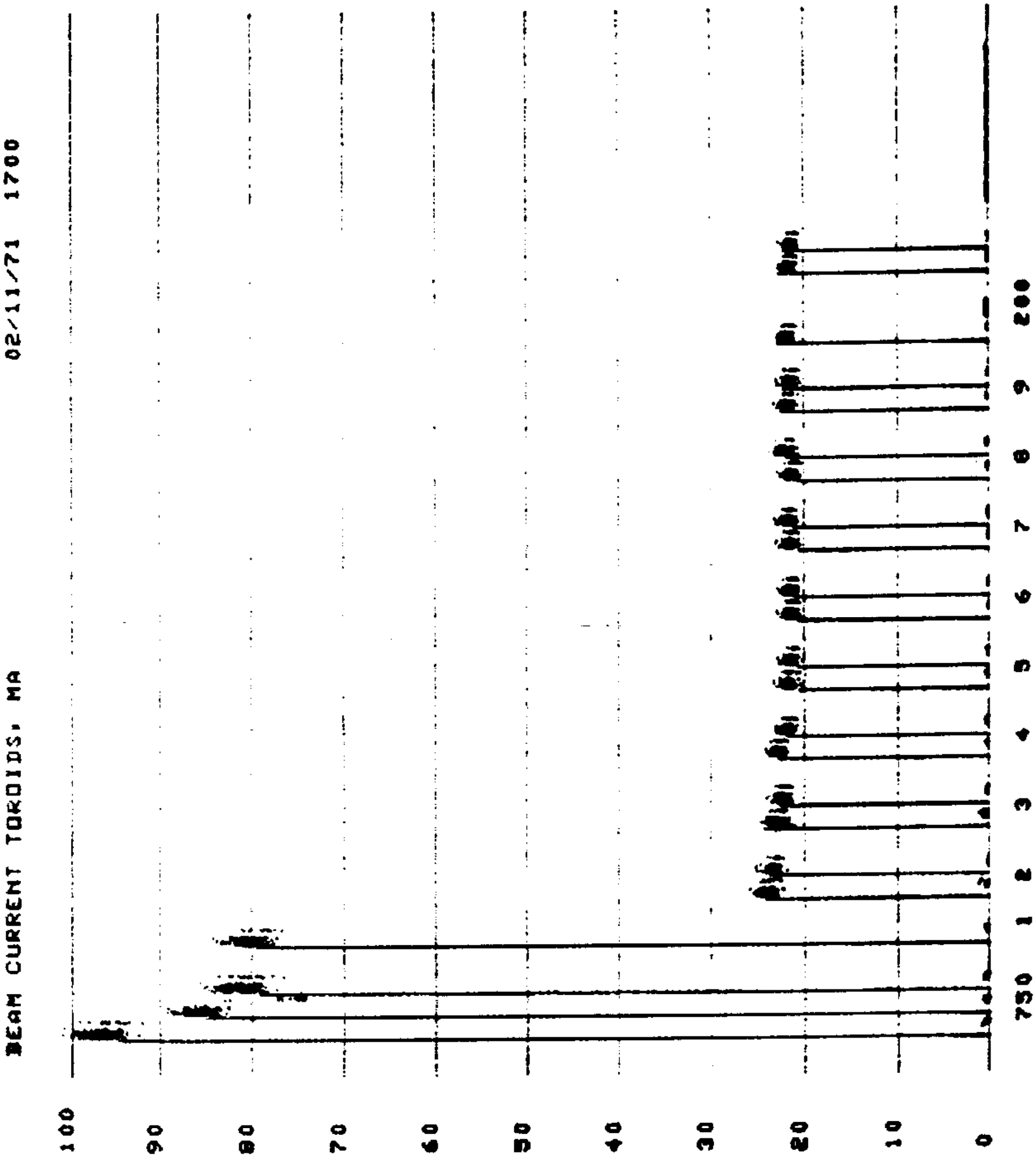
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Fig. 3

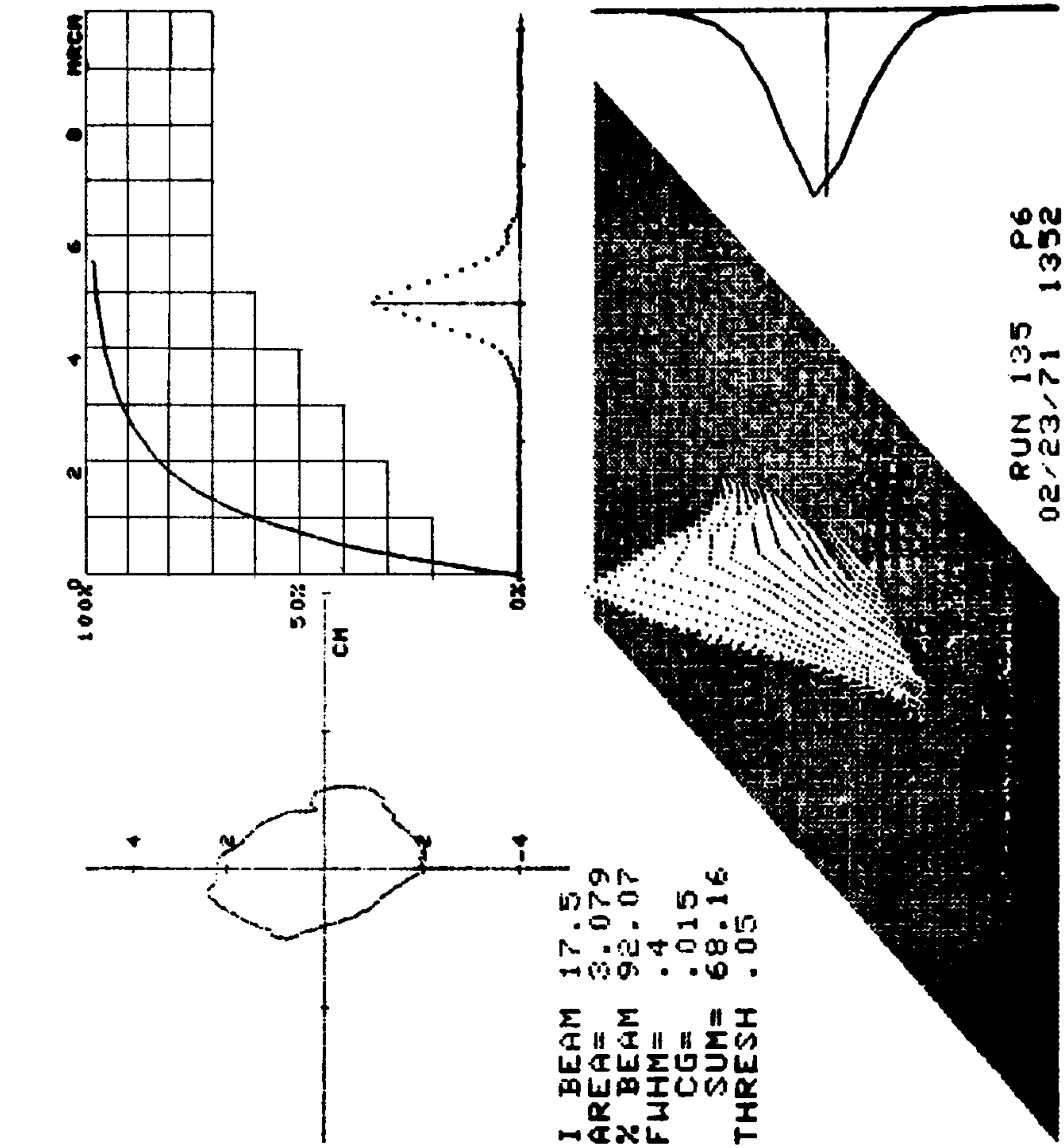
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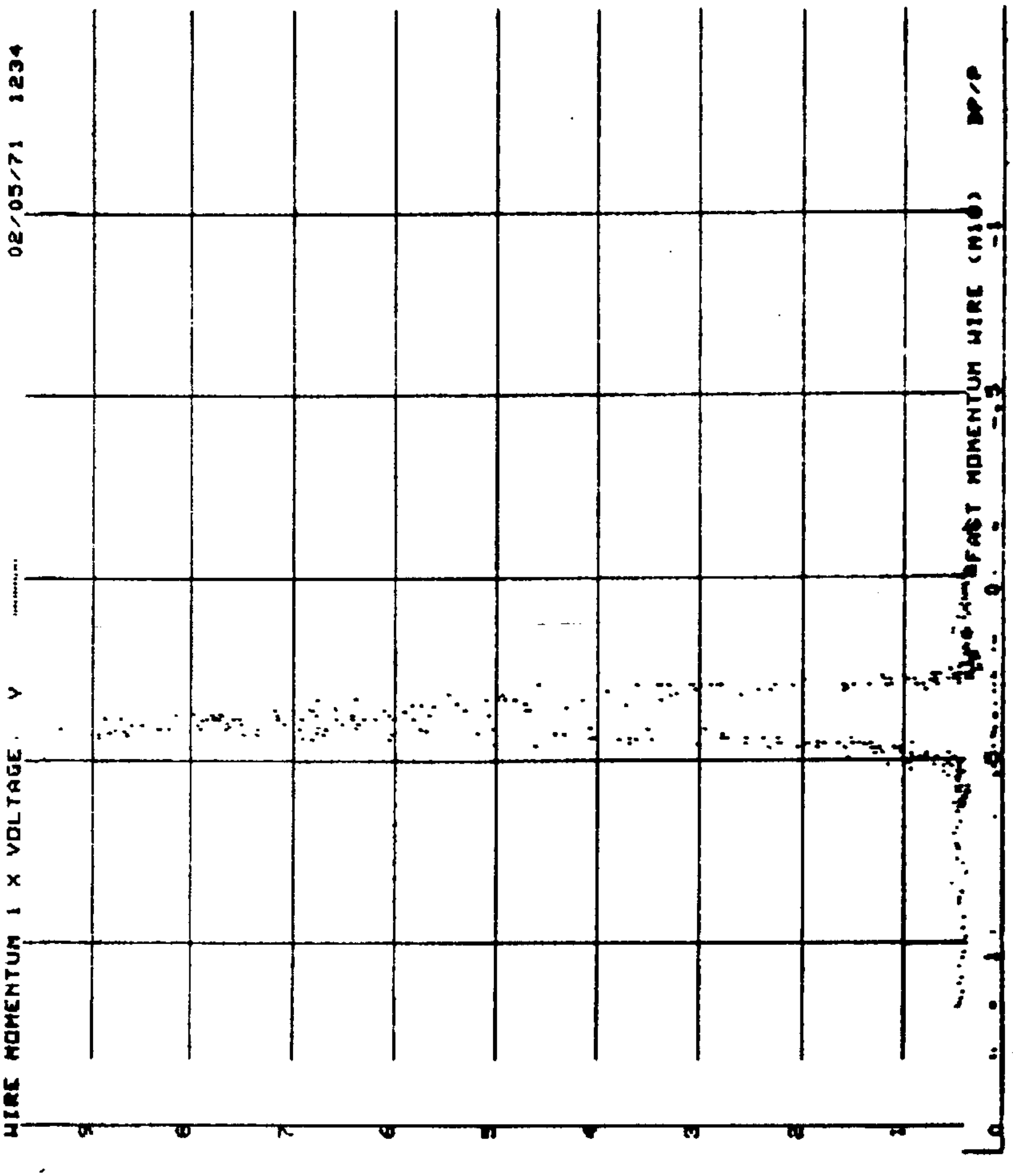
Fig. 4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FAST MOMENTUM WIRE (N10)
DP/P

Fig. 5

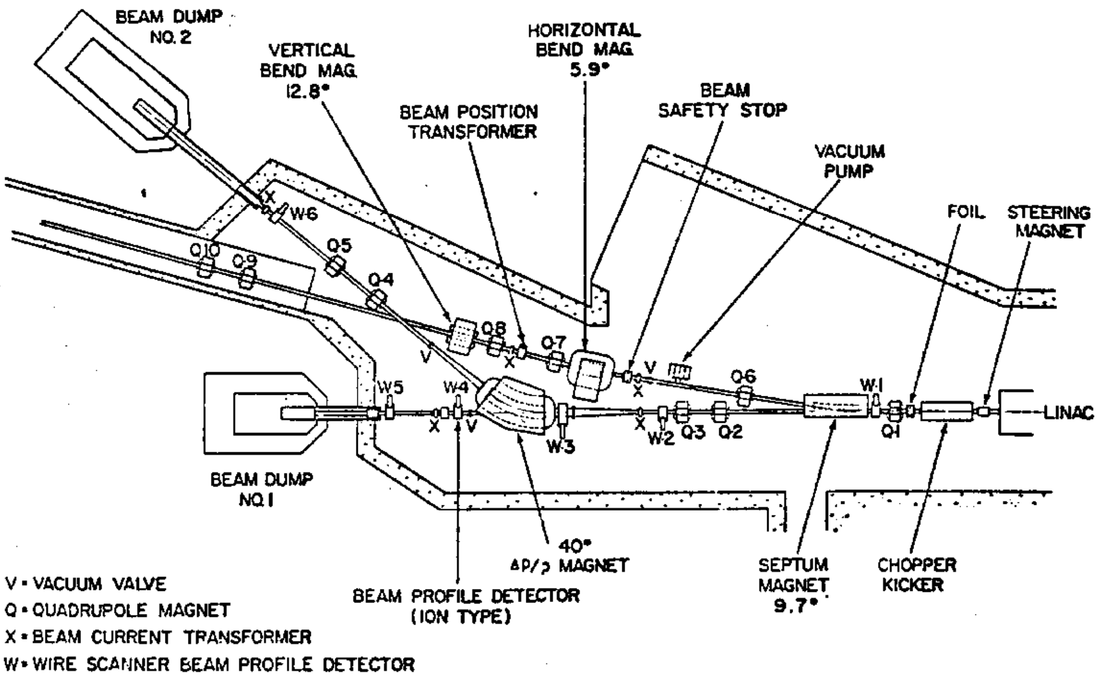

Fig. 6. Layout of the system for measuring the emittance and the momentum spread of the beam from the 200-MeV linac.

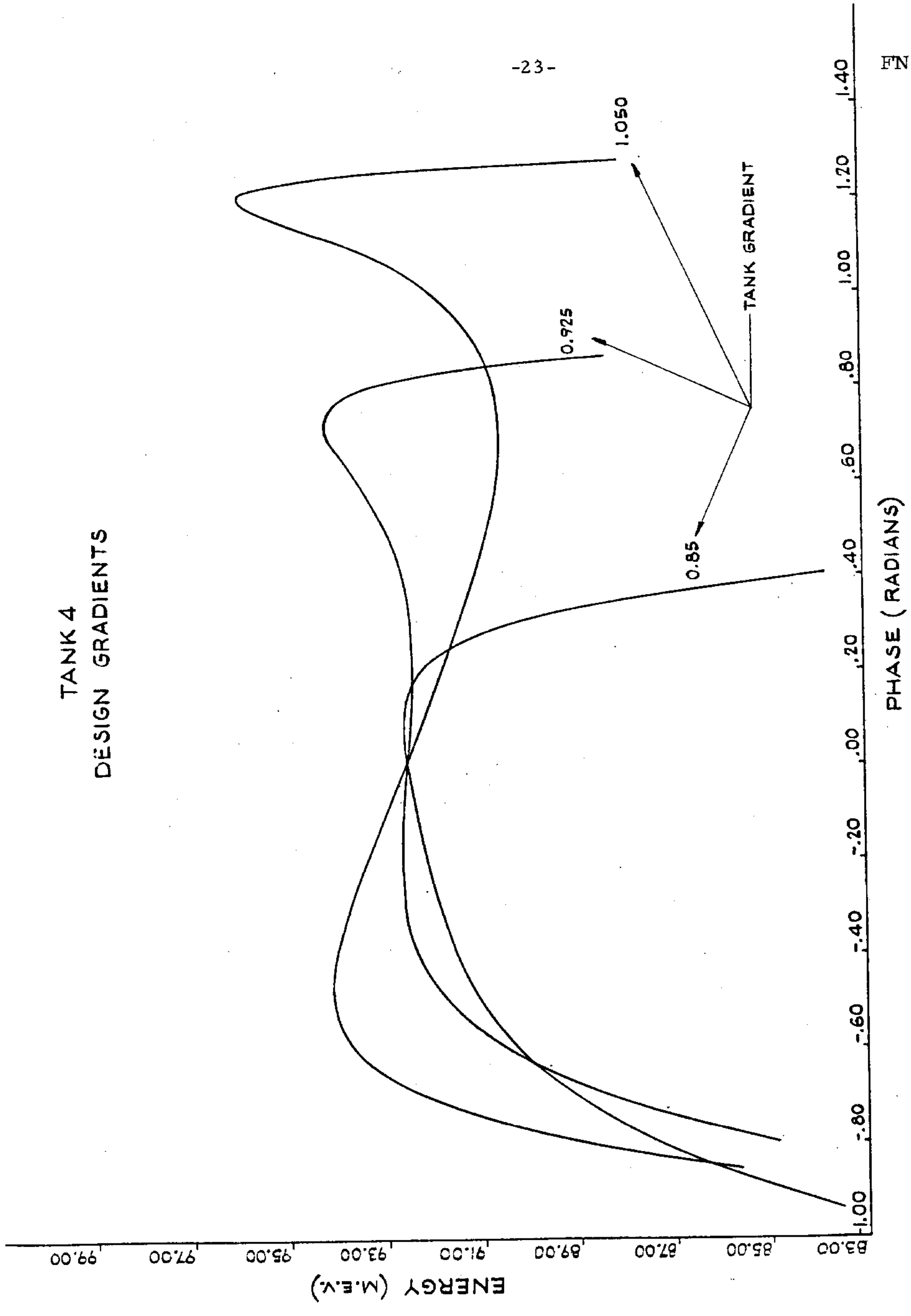
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Fig. 7

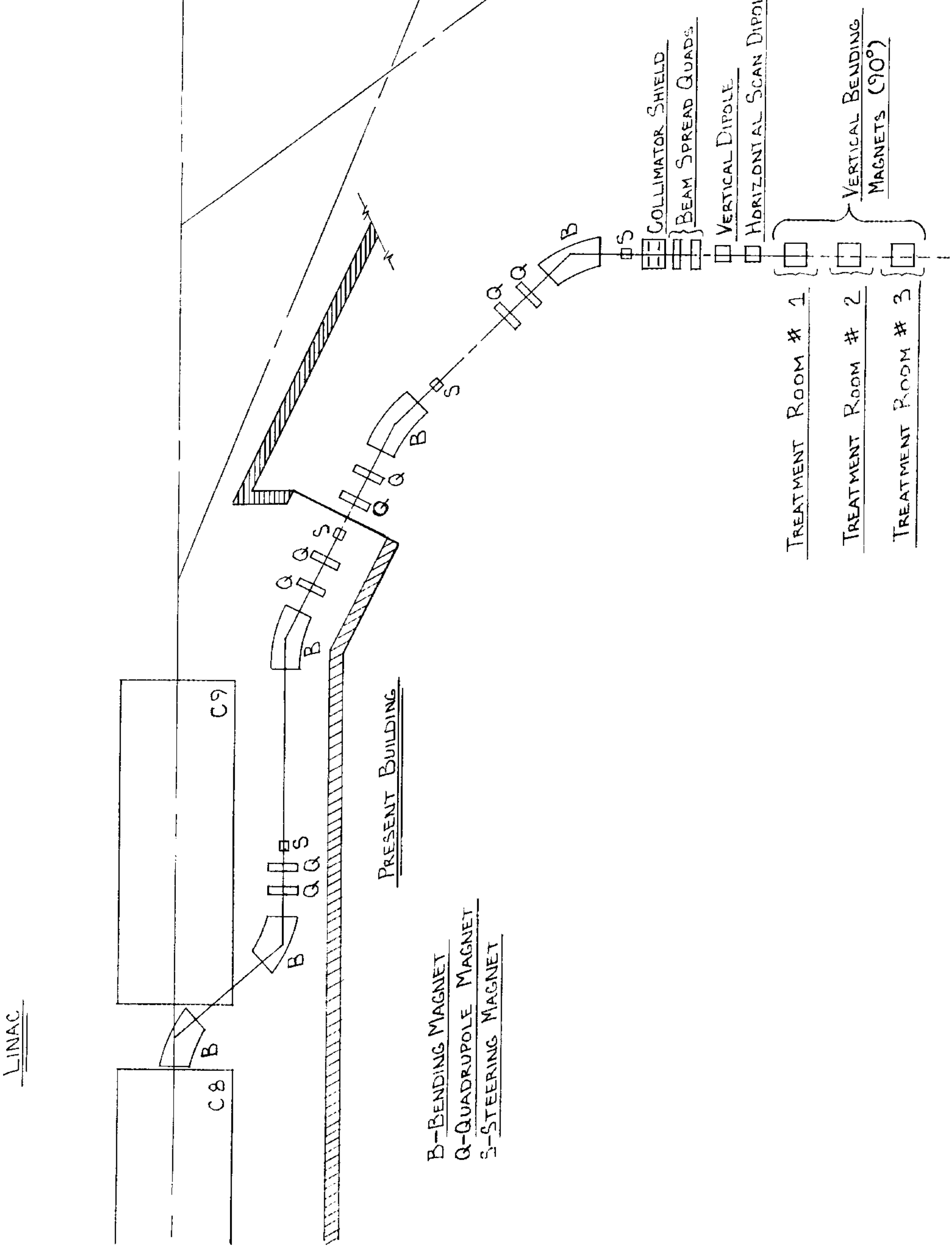

Fig. 8. Not to scale.

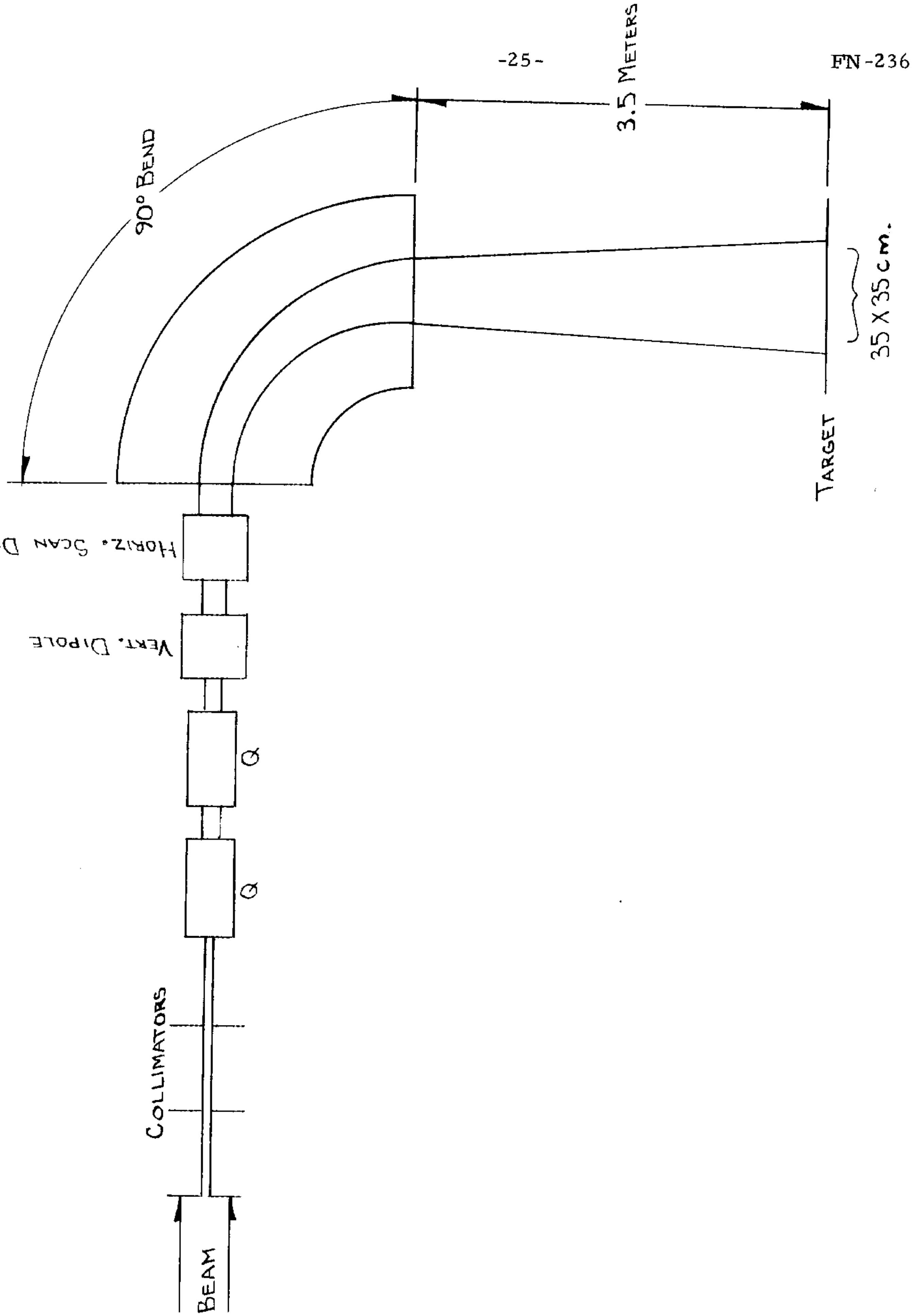

Fig. 9. Not to scale.