LAPORAN AKHIR PROJEK PENYELIDIKAN R&D JANGKA PENDEK USM
R&D/JP - 04

A. MAKLUMAT AM

Tajuk Projek : Kaedah Pengesahan Dos dalam Radioterapi
(Dose Verification Procedures in Radiotherapy)

Tajuk Program : Sinaran Perubatan/Radioterapi

Tarikh Mula : 30.6.96

Nama Penyelidik Utama: Prof.Madya Ahmad Zakaria, 5046330

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PENCAPAIAN PROJEK:

Mengembangkan proses atau teknik baru

1.Dalam perkhidmatan radioterapi sebahagian besar prosedur dan pengiraan dos di dalam tubuh pesakit dilakukan dengan menggunakan komputer sebelum radioterapi dijalankan. Komputer pula menggunakan model matematik dan penghampiran (approximation) yang tertentu untuk mengambilkira parameter pesakit dan ciri-ciri sinaran yang digunakan dalam pengiraan dos. Pengesahan dos yang diramalkan oleh komputer perlu dibuat sebelum komputer ini digunakan dalam applikasi klinikal untuk memastikan semua proses pengiraan dos adalah tepat dan betul. Teknik-teknik untuk mengukur dos secara terus dalam pelbagai situasi untuk mengesahkan sama ada dos pada suatu titik di dalam tubuh pesakit dikira dengan tepat oleh komputer perlu dilakukan.Ini adalah penting untuk memastikan pesakit menerima dos yang betul dan selamat semasa menjalani radioterapi. 6 teknik bertujuan mengukur dos secara terus merangkumi pelbagai geometri telah dijalankan dalam penyelidikan ini.

2.Teknik-teknik ini mengambilkira parameter sinaran yang digunakan untuk pesakit, permukaan tubuh pesakit yang tak sekata, insiden sinaran yang serong dan ketumpatan tisu di dalam tubuh pesakit yang berbeza.Eksperimen dijalankan dengan menggunakan phantom air, phantom pepejal dan 6 MV foton dari alat pemecut (medical linear accelerator).
Dalam semua situasi yang telah dijalankan dos yang diukur melalui teknik ini dan dos yang diramalkan oleh komputer bersetuju dalam lingkungan kurang daripada 2%. Oleh itu program komputer yang kita gunakan iaitu PLATO RTS1.3 telah

disahkan sesuai bagi perancangan dan pengiraan dos untuk perkhidmatan pesakit.

3. Teknik-teknik ini juga boleh digunakan untuk QC berkala terutama sekali apabila komputer dibaikpulih atau selepas peningkatan program dibuat oleh pihak pembekal atau pengguna.Ia juga boleh digunakan dalam projek perbandingan dos (dose intercomparison) untuk semua pusat radioterapi di Malaysia yang menggunakan komputer perancangan yang berlainan program dalam pengiraan dos pesakit.

C.PEMINDAHAN TEKNOLOGI

D.KOMERSIALISASI

E.PERKHIDMATAN PERUNDINGAN

Jenis klien yang mungkin berminat - Hospital kerajaan atau swasta yang memberi perkhidmatan radioterapi untuk memastikan program komputer mereka menghasilkan dos yang tepat sebelum digunakan untuk perkhidmatan pesakit.Pada masa ini aktiviti sebegini adalah mandatori bagi pengguna di hospital di seberang laut seperti US dan UK.

F.PATEN/SIJIL INOVASI UTILITI

G.PENERBITAN HASIL DARIPADA PROJEK

(i) **Laporan/Kertas persidangan atau Seminar**

1.**QA Test on Computer Algorithm in Treatment Planning System** National Conference Medical Physics,12-13 May1997,Kuala Lumpur.

2.**Evaluation of Dosimetric Properties of Bolus Material,** 13th Malaysian-Singapore Radiographers Conference, 15-16 Nov 1997, Langkawi.

H.HUBUNGAN DENGAN PENYELIDIK LAIN

Penyelidik di Makmal Kalibrasi di MINT Bangi. Hubungan dalam aspek dosimetri dan kalibrasi peralatan untuk penyelidikan.

I.SUMBANGAN KEWANGAN DARI PIHAK LUAR

J.PELAJAR IJAZAH LANJUTAN

K.MAKLUMAT LAIN YANG BERKAITAN

Projek ini juga merupakan langkah yang pertama perlu dibuat oleh penyelidik sebelum menjalankan projek penyelidikan lain dalam bidang Radioterapi/Dosimetri yang ada kaitan dengan penggunaan komputer perancangan. Setakat ini seorang kakitangan USM sedang menyediakan cadangan penyelidikan untuk projek Ph.D yang ada kaitan berkaitan dengan projek ini.

Tarikh

24/6/98

Tandatangan

T/TANGAN PENGERUSI
J/K PENYELIDIKAN
PUSAT PENGAJIAN

LAPORAN AKHIR PROJEK R&D JANGKA PENDEK

TAJUK : KAEDAH PENGESAHAN DOS DALAM RADIOTERAPI

PENYELIDIK

AHMAD ZAKARIA, NIK RUSMAN NIK IDRIS
JABATAN PERUBATAN NUKLEAR, RADIOTERAPI &
ONKOLOGI, PUSAT PENGAJIAN SAINS PERUBATAN USM.

Introduction

The aims of radiotherapy are to deliver adequate radiation dose to tumor to achieve local control, and to keep the dose to surrounding and intervening healthy tissues to a minimum. A problem arises because the radiation must penetrate the healthy parts of the body to reach the tumor. In addition, after passing through the tumor, it continues to transverse the body before exiting. Therefore, intervening and surrounding tissues are inescapably irradiated and damaged while tumor cells are destroyed. Generally, the limiting factor in achieving local control is the ability of the adjacent healthy tissues and critical organs to tolerate radiation dose above certain levels and not our ability to deliver an adequate amount of radiation dose to the target. In radiation treatment planning, techniques are devised and arrangements and characteristics of a set of beams are defined with the intent of producing regions of high dose which conform to the shape of the target. Nowadays a significant portion of patient treatments are designed and dose distributions calculated using treatment planning computer. The aim of treatment planning computer is to accurately calculate the dose distribution both within the target volume and in the surrounding tissues by using computational algorithms based on mathematical model that takes into account the shape of the beam, target geometry and tissue inhomogeneities present in the patient. In general, the presently available methods of absorbed dose calculation for irregular field and for a heterogeneous medium are only approximate. The dose distribution in a patient is usually computed using central axis depth dose data in conjuction with dose profiles measured at several depths over a range of field sizes. The radiation beam data refer in one way or another to measurements in a homogeneous water phantom under reference conditions, i.e., beams of square cross-section, symmetrical energy fluence, and standard distance to and normal incidence on a flat surface. Tissues which differ from water in composition (in term of electron density), e.g. lung, bone, and fat, perturb the dose at a point in patient by modifying the primary radiation as well as the scatter component of the radiation beam. The various algorithms that have been developed to correct for these effects all suffer in some degree in not being a 3 dimensional computation which can take into account the composition, size, and shape of the inhomogeneity. Before such a dose calculation algorithm can be placed into routine clinical use, it must be carefully evaluated and verified by the users (1, 2, 3). The purpose of the algorithm evaluation can be two-fold. First, it serves to verify the correctness of the input data. Second, it also provides users with some insights into the accuracy and limitations of the algorithm.To ensure the safe and accurate delivery of the prescribed radiation dose the dose computation algorithms should be checked against measured data before being used for patient treatment plans .

In our department we have been using 2-D Nucletron PLATO External Radiation Treatment Software (PLATO RTSv1.3) for treatment planning and photon beam calculations. The algorithms are based on a three pencil beam model that describe the primary and scattered radiation (4). This model takes oblique incidence, irregular fields, beam blocks and inhomogeneities into account. The photon dose calculation for all clinical fields is based on a correction factor which is calculated for each point with

Dose Verification Procedures in Radiotherapy

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Summary

In radiotheraphy the accuracy of the radiation dose to be delivered to patient is vital. In the current practice the dose to be delivered by the treatment machine is calculated using computer planning system which utilised computational algorithms based on mathematical model that takes into account the shape of treatment beam, target geometry and tissue inhomogeneities present in the patient. To ensure the safe and accurate delivery of the prescribed dose the dose distributions predicted by the system must be validated before use in clinical setting. The aim of this work was to establish simple and practical test cases that would permit comparison of computed doses with measured values in order to verify the accuracy of the dose computation process in our treatment planning system. In our study the dose at selected points for each test condition consisting of beam-phantom configuration irradiated with 6MV photon beam was computed with Nucletron PLATO RTS treatment planning computer using pencil beam algorithms. The computer predicted values were compared with dose values obtained from measurements. Based on 6 MV input beam data, geometry of the phantom and the chosen treatment set up, the computer generated the isodose curves for each test condition.The dose was then prescribed at a chosen isodose line.The computer then calculated the treatment monitor units for the machine and also the absolute dose at any selected point in the phantom for each test condition. Using the same monitor unit calculated and the same test condition the photon beam was then applied to the phantom and the absolute dose at selected points was determined by measurement based on the charges collected by ionization chamber.The charges collected at the selected points were converted to absolute dose using American Association of Physicists in Medicine Task Group 21 (AAPM TG 21) Protocol.The test cases carried out in this study include : (a) open square field and normal incidence; (b) rectangular field, wedged, oblique incidence and non-flat surface; (c) open square field with lung and bone inhomogeneities. In most test cases dose variations were less than 2%. The variation between measured and calculated data for all the test conditions ranged from 0.3% to 6.9%. Our results showed that the algorithms (pencil beam) in the planning computer gave acceptable accuracy for our test cases. The test conditions that we have established are simple to carry out and well-suited as part of QA procedures for treatment planning system before use in clinical setting.

(3) Off-axis profiles for different depths for the maximum wedged field size for the different wedges (max. 4 depths).
(4) One PDD for the largest field size for different wedges (wedge PDD).
(5) An off-axis profile for the largest field size (Flattening filter profile).

Point measurements in air

Point measurements in air for different field sizes (collimator scatter, output factors) with the cylindrical perspex phantom (max. 10).

Test cases

The test cases were set up using water phantom, polystyrene phantom and solid water phantom utilising 6 MV photon produced by Siemens Mevatron Model MXE 6740 linear accelerator. The water phantom (50cmx50cmx50cm) has automated field scanning support mechanism that can transport a measuring probe (ionization chamber) with great accuracy and precision. The polystyrene phantom (Nuclear Associate Depth Dose Phantom) has built-in openings to accept measuring probe situated at various depths (Figure 1). The dose at selected points in the phantom was determined using calibrated Scanditronik cylindrical ionization chamber (RK 8305; volume=0.12cm^3 ; diameter= 4mm) connected to Victoreen Electrometer model 525 for charge measurement.

In each of the test cases described below the first thing that was done was treatment planning using our computer system. In the test case using water phantom, the outline of the phantom was drawn in the computer using digitizer provided. For test case utilising polystyrene phantom, CT scan (Siemens Somatom HiQ Scanner) was carried out and then data was transfered to the computer for planning using floppy disk. Based on the geometry of the phantom , the chosen treatment set up for each of the experiment and the input beam data, the computer generated isodose lines in a particular plane in the phantom. The dose was then prescribed on a chosen isodose line. The computer then calculated the machine treatment monitor unit (MU) and the dose value at any point in the phantom. For a particular treatment set up the beam was then applied to the phantom using the same monitor units calculated. The charges produced at selected points during irradiation were measured by the ionization chamber and electrometer system. Using the average value of the charges from electrometer readings taken with positive and negative polarities the dose at selected points in the phantom was then determined using AAPM TG 21 protocol (5). The dose measured in polystyrene phantom was then converted to the dose in water using the same protocol. The calculated and the measured dose in water for each set up were compared using percent difference.

The coordinate system used for data measurements was defined as follows: the +z direction is the same as the direction of the beam; the +y direction is toward the gantry; and the +x direction is such as to make the coordinate system left-handed. The coordinate

pencil beam method, and multiplied with the dose in reference situation. The correction factors take into account the deviation of the actual (to be planned) configuration from the standard (measured) configuration. The reference situation is obtained from interpolation of the measurements which comprise Percentage Depth Dose, beam profiles and output factors. The aim of this work was to establish simple and practical test cases consisting of beam-phantom configurations that simulated various patient anatomic structures and beam geometries in order to verify the dose predicted by the computer against measurement.

Materials and Methods

Test cases representing 6 different treatment planning conditions to evaluate the accuracy of the dose computation algorithms were carried out in this study. The beam characterization data were first entered into the treatment planning system. Next, treatment plans were prepared for the 6 test cases. Subject anatomy can be entered into the computer via digitizer tablet or directly from CT scanner via floppy disk for planning purposes. Tissue densities can be assigned by the user to the contoured volumes like a lung or a bone for heterogeneity corrections. Finally, results calculated from the treatment planning system were compared with the measured data.

A. Beam data input for treatment planning computer

A Nucletron water phantom, a Scanditronik cylindrical ionization chamber and a cylindrical perspex phantom was used to obtain beam data needed by the computer for computation. The following data were input in the Nucletron PLATO planning System and stored as photon beam files.

Point measurements in water phantom

(1) A calibration measurement for the standard set up: SSD=100 cm, at a depth of maximum dose, for 10 x 10 cm field size.
(2) Point measurements in water for different field sizes (total scatter output factors) with the water phantom (maximum 10).
(3) Point measurements in water for one reference or more field sizes with different trays (tray transmission factor).
(4) Point measurements in water for one reference or more field sizes with different wedges (wedge factor).
(5) Point measurements in water for different blocks (block transmission factor).

Scans in water phantom

(1) Percentage Depth Dose (PDD) for different field sizes (max.12)
(2) Off- axis profiles for different field sizes and various depths (max. 4 depths, max. 20 field sizes).

Experiment 4 (Test case 4): 3 cm high 90 degrees stepped polystyrene phantom, oblique incidence, wedged and at standard SSD

The purpose of this experiment was to check the computer algorithm handling oblique incident, non- flat surface and correction for wedge. Figure 8 shows the experimental set up . The selected points for measurements and the field size were the same as experiment 3 except for the wedge and the angle of incidence. The beam hit the upper surface of the phantom at 14 degrees using 30 degrees wedge. The central axis of the beam met the upper surface 2 cm from the edge of the step. Figure 9a to Figure 9c show the computed isodose lines including the measurement points for this case.

Experiment 5 (Test case 5): Bone Inhomogeneity

This experiment was designed to check the capability of the available computational methods to predict the dose distribution perturbations arising from the presence of bone tissue inside solid water phantom. 10 cm x 10 cm open beam with SSD = 100 cm, incident on a slab 30 cm x 30 cm phantom, consisting of 3 cm thick solid water, 2 cm thick bone phantom (density = 1.79), followed by 7 cm thick solid water (Figure 10). Figure 11 shows the predicted dose distribution along the central axis of the beam and also the measurement points on this axis.

Experiment 6 (Test case 6): Lung Inhomogeneity

The objective of this test was to check the accuracy of the computational algorithm in taking care of the presence of lung tissue inside solid water phantom. 10 cm x 10 cm open beam with SSD = 100 cm, incident on a slab 30 cm x 30 cm phantom, consisting of 3 cm thick solid water, 1 cm thick lung phantom (density = 0.29), followed by 7 cm thick solid water (Figure 12). Figure 13 shows the predicted dose distributon along the central axis of the beam and also the measurement points on this axis.

Results

The results of the studies are shown in Table 1 to Table 6.

Discussion and Conclusion

We have done 6 test cases representing different aspects of the dose computation process to verify the computational algorithm in our treatment planning computer. These test conditions resembled some of our common treatments in delivering the prescribed dose to patients. Results from Table 1 to Table 6 have shown that the agreement between calculated and measured data ranged from 0.3% to 6.9% depending on test case and

of (0cm,0cm, 0cm) is the point where the central axis of the beam meets the surface of the phantom.

Experiment 1 (Test case 1): Water phantom, normal incidence, standard SSD.

This is the most fundamental test of any radiation dose calculation algorithm i.e its ability to predict the measured dose distribution in water phantom at the standard treatment distance. It is the ability of the computer to compute dose within beams similar to input data conditions. In this case 10 cm x 10cm field with 100cm SSD and the beam incident normally was chosen (Figure 2). The MU of 140 was applied based on prescribed dose of 100cGy at 70% isodose line. Figure 3 shows the points in the y = 0 plane (central plane) that were chosen for measurements and the computed isodose lines. The coordinates of the points are: A= (-3.2 cm, 0 cm, 5 cm), B = (8.8 cm, 0 cm, 7.7 cm), C = (0 cm, 0 cm, 8.8 cm) and D = (2.2 cm, 0 cm, 17.4 cm).

Experiment 2 (Test case 2): Water phantom, multiple fields, oblique incidence, wedges, standard SSD.

The purpose of this experiment was to verify the ability of the software to sum the dose from multiple fields, to handle oblique incidence beams and to take account of wedge and scatter corrections. Figure 4 shows the set up for this study. Beam 1 was 27 deg from central axis with 30 deg wedge and beam 2 was 335 deg from central axis with 45 deg wedge. Both field sizes are 12cm x 14 cm.The MU's of 225 and 364 for beam 1 and beam 2 respectively were applied based on prescribed dose of 200cGy at 70% isodose line. The points of measurements are in the central plane (y = 0) with A= (2.3 cm, 0 cm, 2.4 cm), B = (-4 cm, 0 cm, 2.5 cm), C = (6.9 cm, 0 cm, 7.2 cm) and D = (-6.5 cm, 0 cm, 6.8 cm) as shown in Figure 5 including the computed isodose lines.

Experiment 3 (Test case 3) : 3 cm high 90 degrees stepped polystyrene phantom, normal incidence at standard SSD

This experiment was designed to check the computer algorithm handling non- flat surface. Figure 6 shows the set up of this study. The beam with field size of 13cm x 8cm and MU of 139 based on prescribed dose of 100cGy at 70% isodose line was applied normally to the suface of the phantom. The upper surface of the phantom is at 100cm SSD. The points of measurements are in three different planes: A is in y = 0 plane, B is in y = -1.5 plane and C is in y = -3.0 plane. The coordinates for the three points are: A = (1 cm, 0 cm, 6.5 cm), B = (7 cm, -1.5 cm, 8 cm) and C = (-5 cm, -3.0 cm, 8 cm). Figure 7a to Figure 7c show the computed isodose lines and the chosen measurement point in the respective plane.

It is worth mentioning that the selection of test cases in our study do not cover a wide range of clinical procedures. We also did not make an extensive point measurements in each of the experiment for example making measurements of dose distributions in a particular plane in the phantoms and compare with calculated data. We have chosen only few points for measurements in a particular plane in each setup. This work was meant to be a routine check and so it should be simple to do using minimum material available and does not involve many measurements. Based on our data we have shown that the pencil beam algorithm in PLATO-RTS produced an acceptable accuracy for all the test cases in this study.

treatment geometry. On the average the overall agreement was within 2% which is the acceptable criteria for accuracy in treatment planning system (3). It is to be noted the agreement was more than 5% for point B in experiment 1, point B in experiment 4, and point A in experiment 5. From Figure 3 it can be seen that point B lies outside the primary beam and it is to be expected that the computational model is not accurate at this point. In experiment 4 the agreement between measured and calculated data at point B was 6.7%. From Figure 9b we find that point B is in the region of high dose gradients which is the edge of the beam (penumbral edge) where the value of the dose changes rapidly with distance. Figure 11 shows that point A in experiment 5 is at the interface between bone and water. It is well-known that the 2 dimensional dose computational algorithms available commercially at the present time do not adequately account for the dose in transition regions, e.g. , the buildup region (high dose gradient) or near heterogeneuos tissue interfaces within the body (6). Recent works have shown that in the situations where the inhomogeneities were present the agreement between measured and calculated data was only between 10% to 19% for depth dose point values lying under the inhomogeneities (7, 8).

Test case 4 was the most complex treatment set up since it involved non-flat surface phantom, oblique beam incidence and the primary beam was partialy block using blocking metal device (wedge). The measured depth dose points were situated in different planes parallel to beam axis. Data have shown that the agreement in this case was between 2.5% to 4.6% for points situated in the low dose gradient. We believed that the main source of error came from the positioning of the external probe during measurement. We have observed that by moving the pointer in the computer 0.5 cm around the point of interest the calculated dose value could change from 2% to 3%. Since the probe has external diameter of 0.7 cm we would expect the error in positioning the center of the probe in the phantom during measurement to be at least of this order. Taking this into account our results showed good agreement between measured and calculated data.

It is to be noted that we have used CT scan data of solid phantom for tretment planning in experiment 3 and 4. Data obtained was used to outline the geometry of the subject and identified the point of measurements for dose computation. In a way the results from this work verified that the algorithm was able to read and use the CT data for planning and calculation purposes. This is important to know because CT data are routinely utilised for planning the treatment in order to locate many anatomical sites within a patient for inhomogeneities corrections e.g., in the breast cancer treatments to know the dose going into the lung area. It was mentioned earlier that the pencil beam model used various measured data for calculation purposes i.e the model is not totally theoretical. This would mean that the input data needed should be accurate for the computer to predict the dose distribution. Our work has confirmed that the input data that we have measured for the computer and the beam calibration that was carried out were accurate for clinical application.

Table 1. Results of experiment 1 (Test Case 1)

Points	Calculated (cGy)	Measured (cGy)	% Difference
A	122.1	124.2	1.7
B	5.1	5.4	5.7
C	100.0	101.0	0.9
D	62.9	62.3	0.9

Table 2. Results of experiment 2 (Test Case 2)

Points	Calculated (cGy)	Measured (cGy)	% Difference
A	248.5	251.8	1.3
B	207.7	213.9	2.9
C	112.2	108.9	2.1
D	90.0	92.8	3.1

Table 3. Results of experiment 3 (Test Case 3)

Points	Calculated (cGy)	Measured (cGy)	% Difference
A	111.1	107.1	3.6
B	113.1	112.4	0.6
C	33.1	33.0	0.3

Table 4. Results of experiment 4 (Test Case 4)

Points	Calculated (cGy)	Measured (cGy)	% Difference
A	75.5	73.6	2.5
B	44.4	47.7	6.7
C	79.6	75.9	4.6

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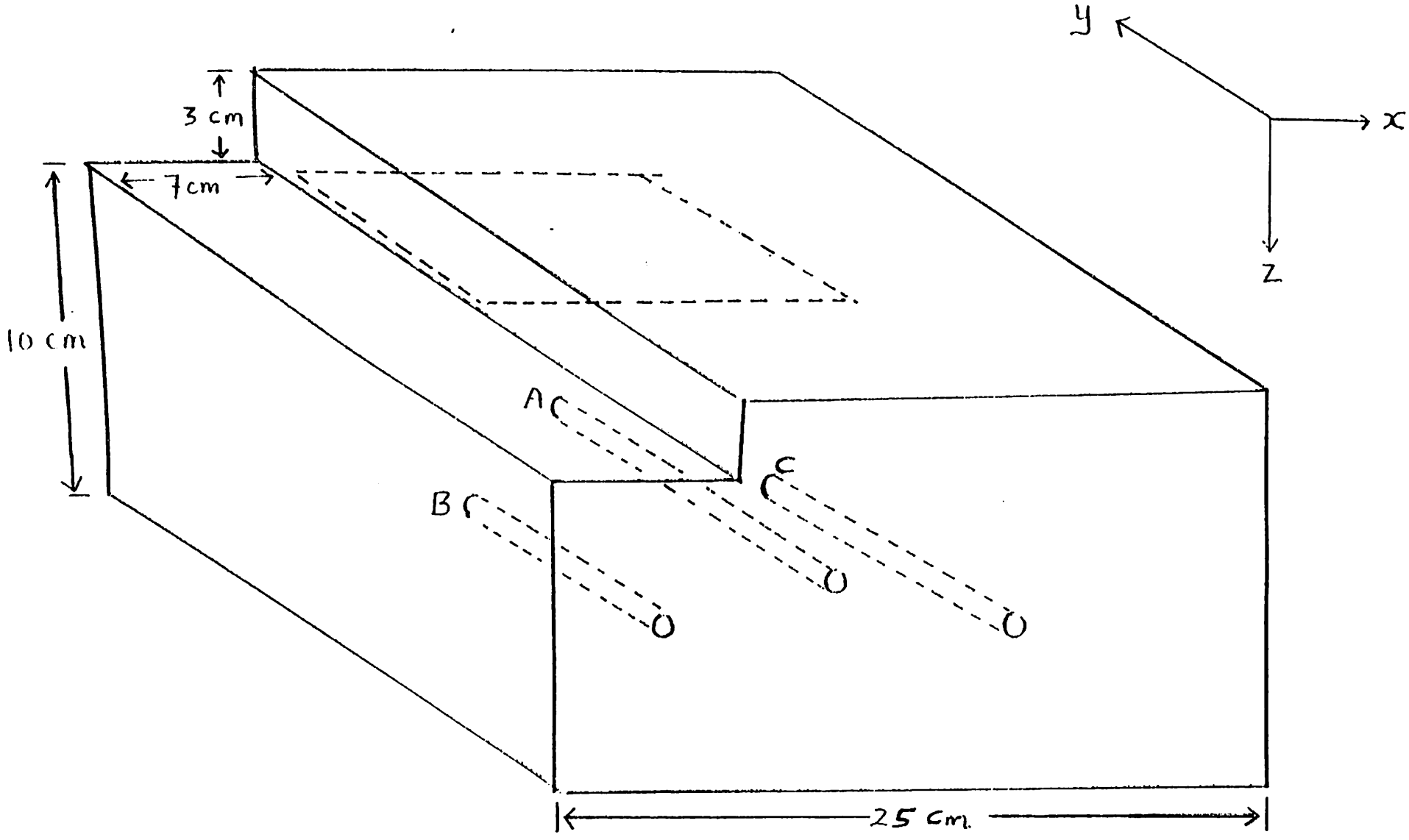

Figure 1. Polystyrene phantom used in the study showing the measurement points at various depths situated in different planes.

Table 5. Results of experiment 5 (Test Case 5)

Points (Depth)*	Calculated (cGy)	Measured (cGy)	% Difference
A (Interface)	120.5	112.1	6.9
B (1 cm)	110.8	108.9	1.7
C (3 cm)	100.0	98.0	2.0
D (6 cm)	84.1	83.1	1.1

* Depth below bone phantom

Table 6. Results of experiment 6 (Test Case 6)

Points (Depth)*	Calculated (cGy)	Measured (cGy)	% Difference
A (Interface)	127.2	128.3	0.9
B (2 cm)	118.7	116.2	2.1
C (7 cm)	91.2	90.1	1.2

* Depth below lung phantom

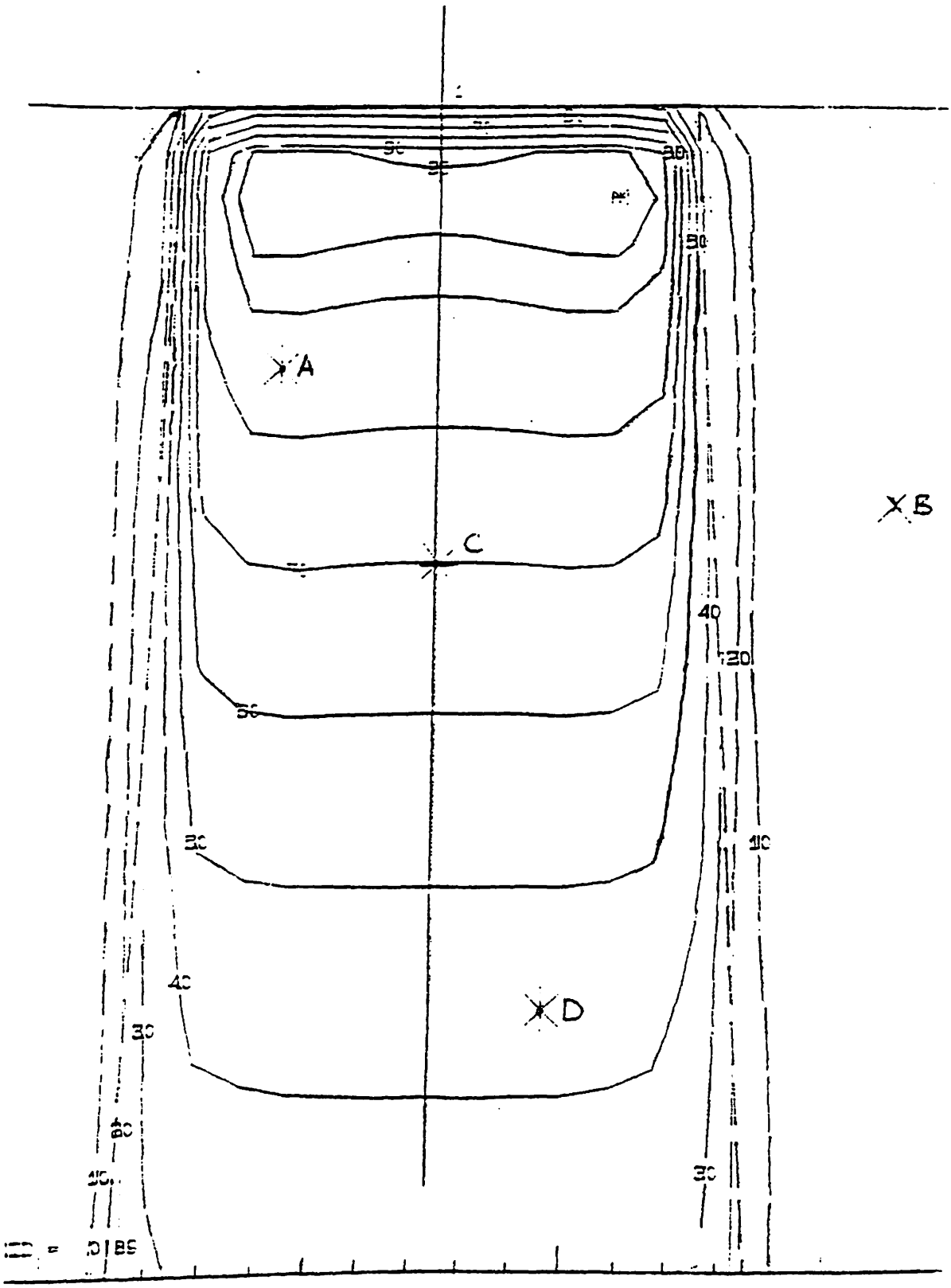

Figure 3. Computed isodose lines in the central plane of the water phantom including measurement points A, B, C and D in experiment 1.

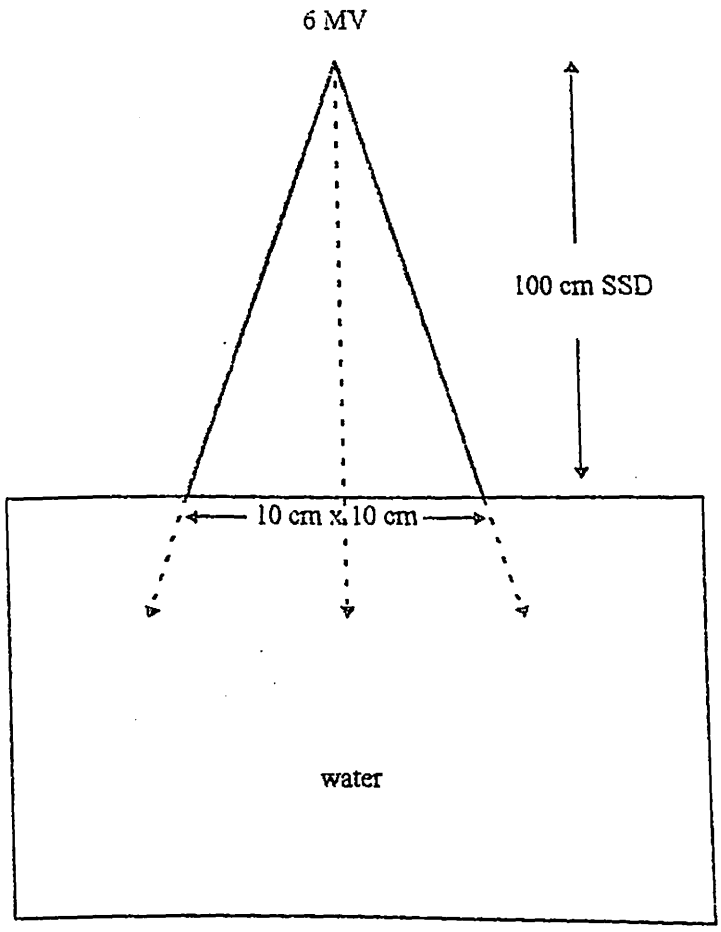

Figure 2. Set up of experiment 1

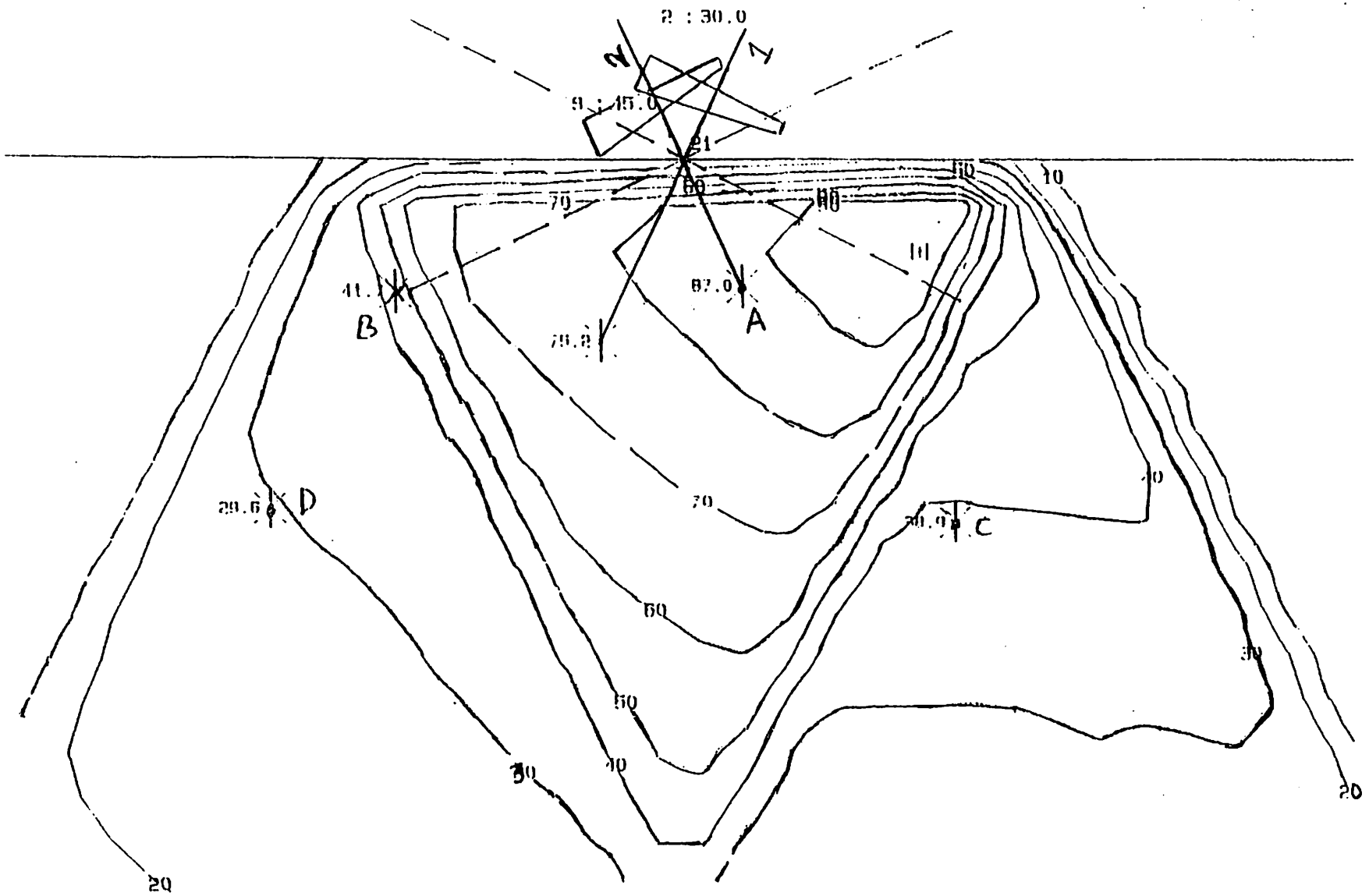

Figure 5. Computed isodose lines in the central plane of the water phantom including measurement points A, B, C and D in experiment 2.

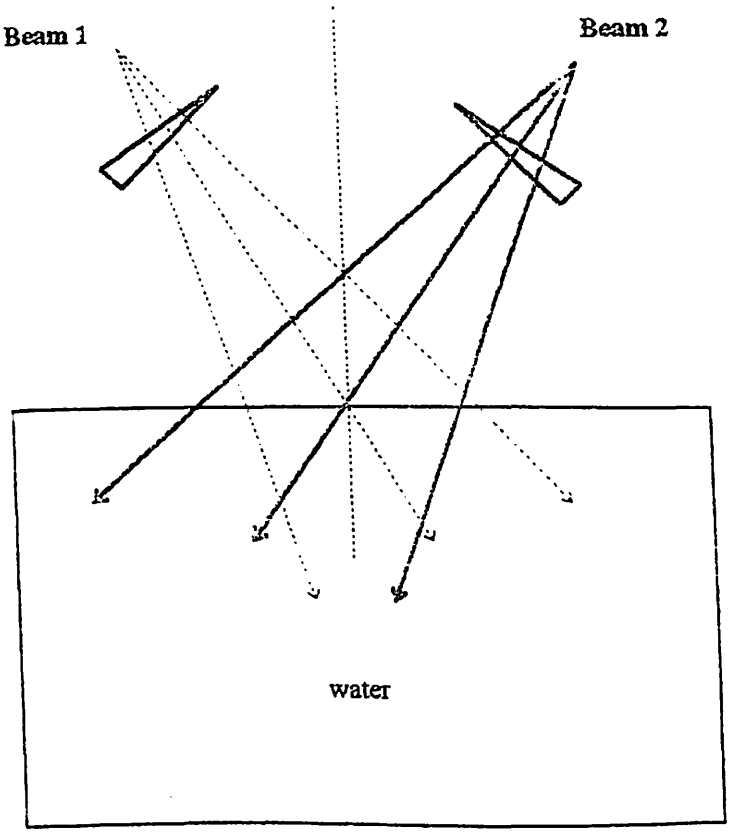

Figure 4. Set up of experiment 2

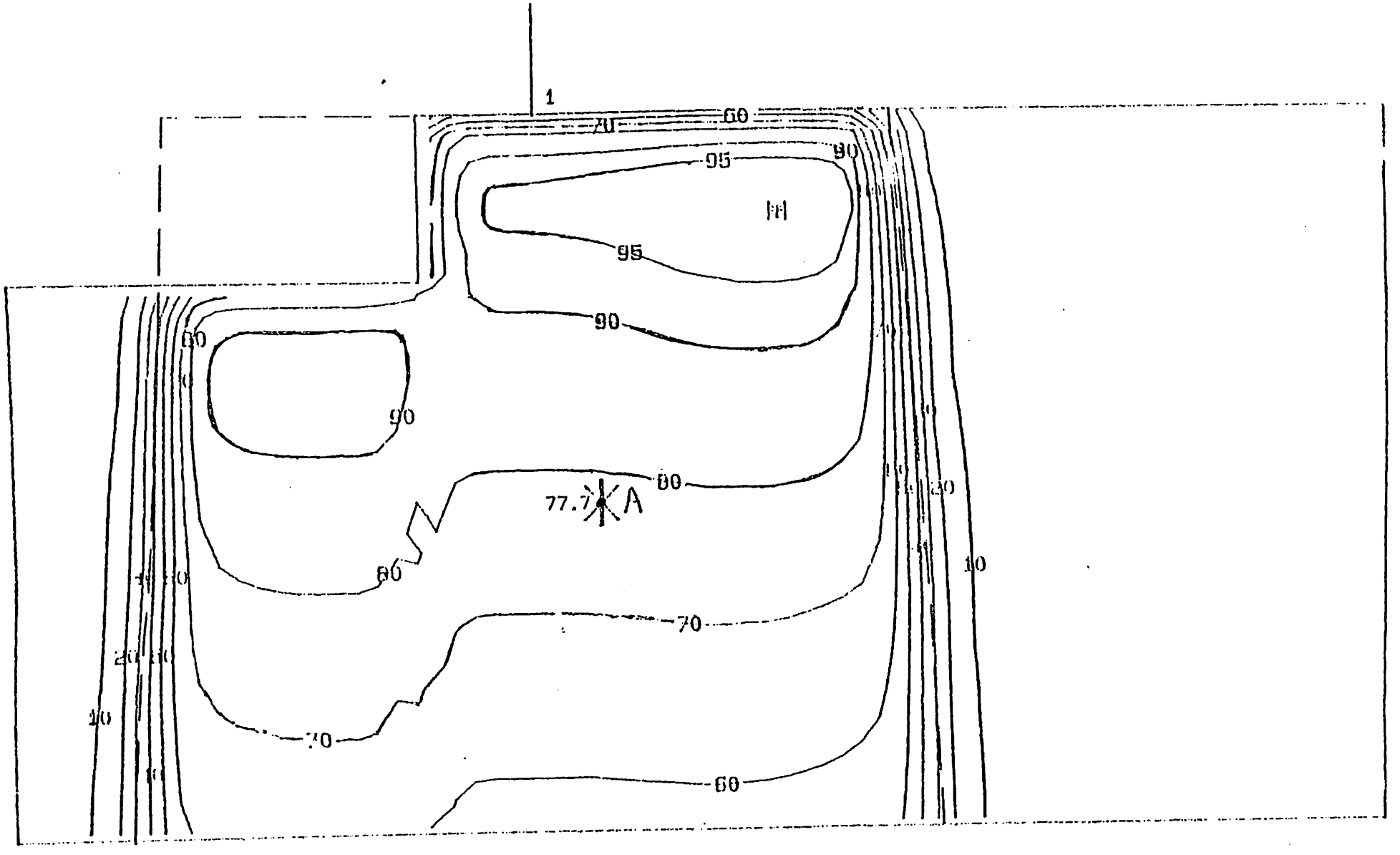

Figure 7a. Computed isodose lines in Y = 0 plane which contains point A in polystyrene phantom in experiment 3.

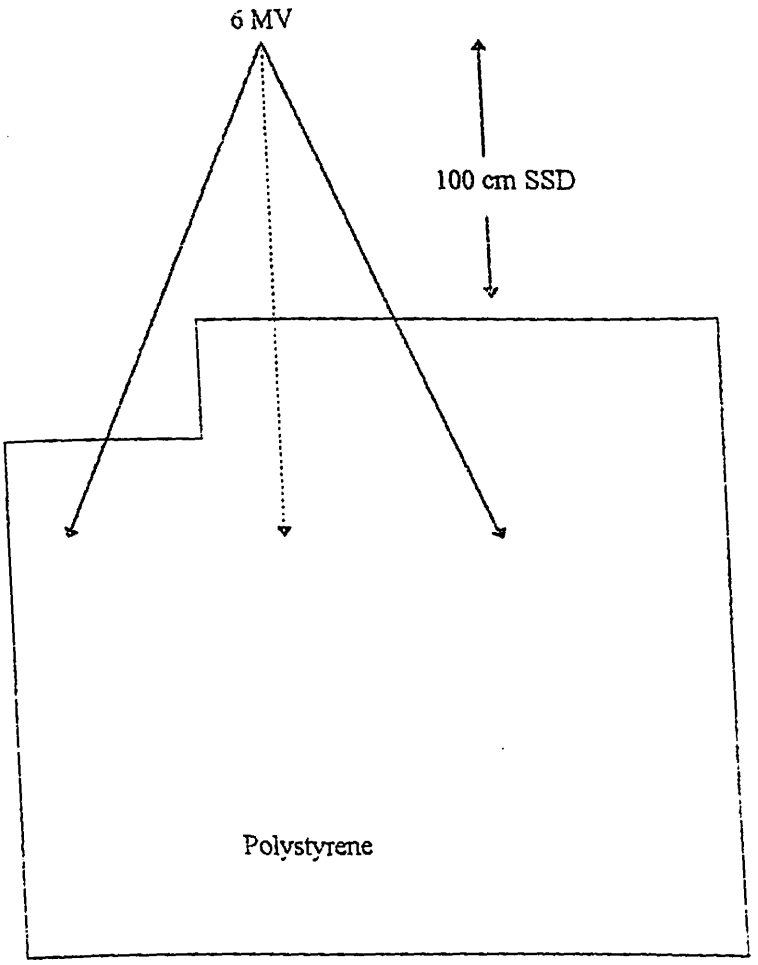

Figure 6. Set up of experiment 3

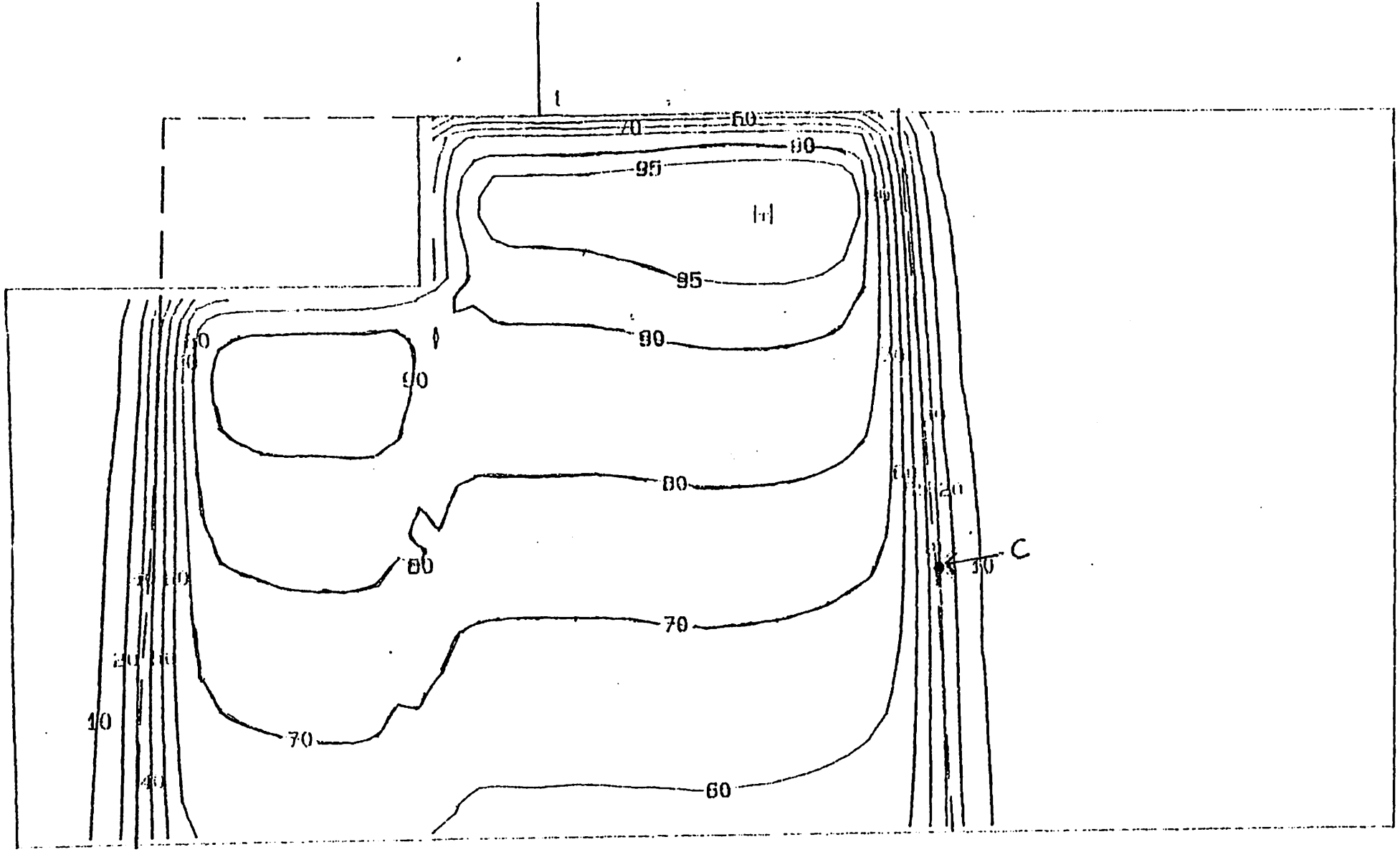

Figure 7c. Computed isodose lines in Y = - 3.0 plane which contains point C in polystyrene phantom in experiment 3.

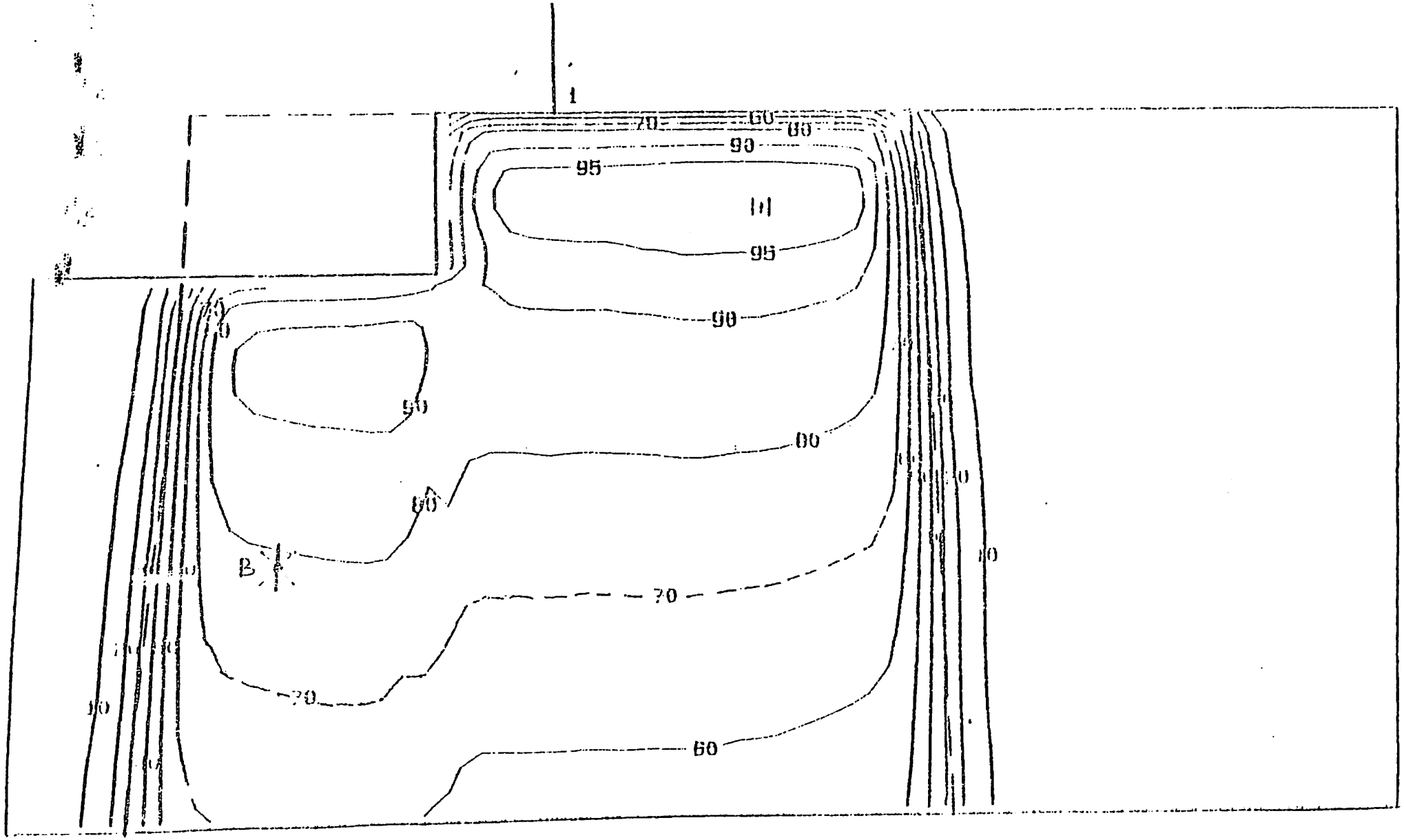

Figure 7b. Computed isodose lines in Y = - 1.5 plane which contains point B in polystyrene phantom in experiment 3.

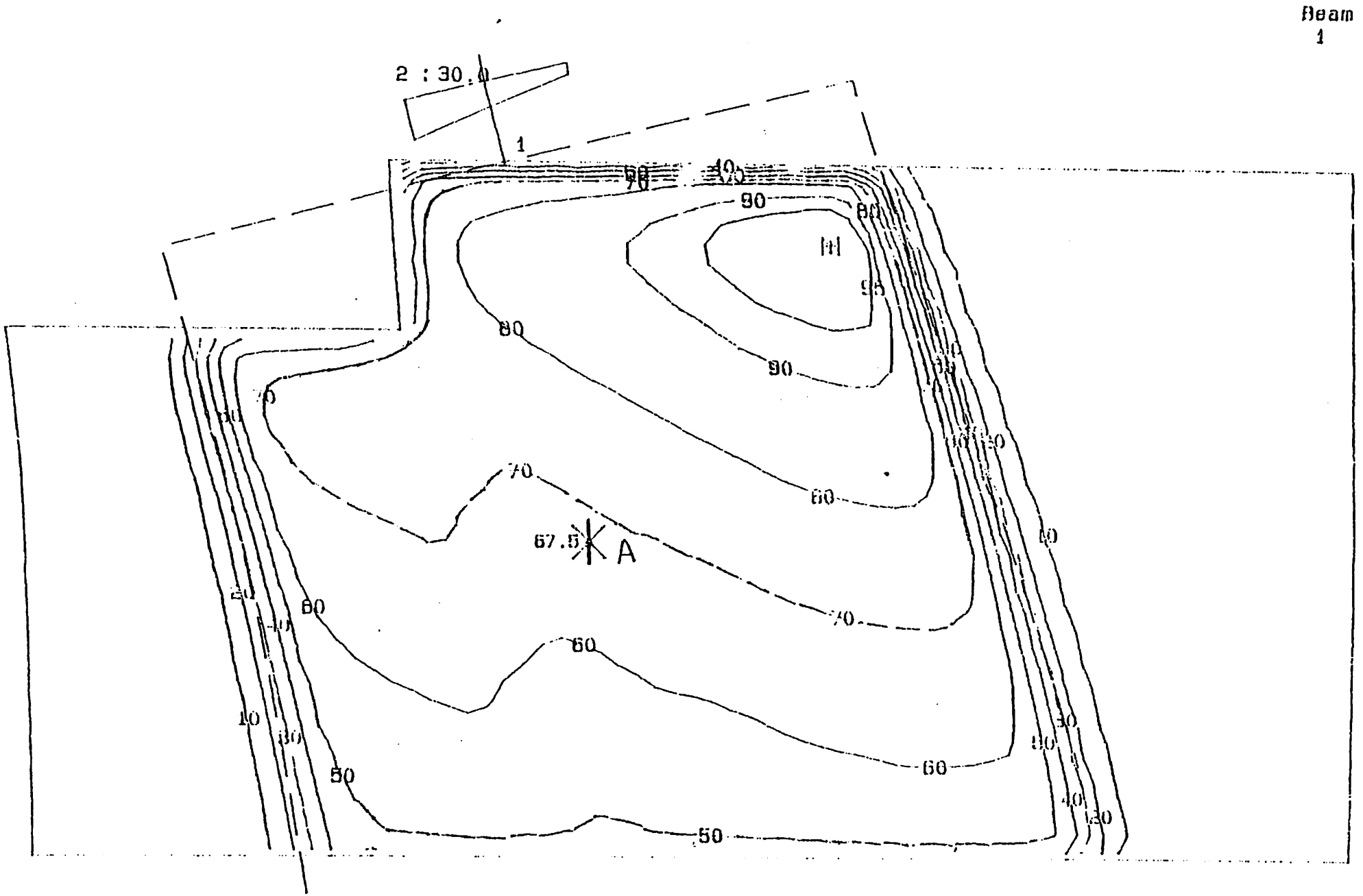

Figure 9a. Computed isodose lines in Y = 0 plane in polystyrene phantom including point A in experiment 4.

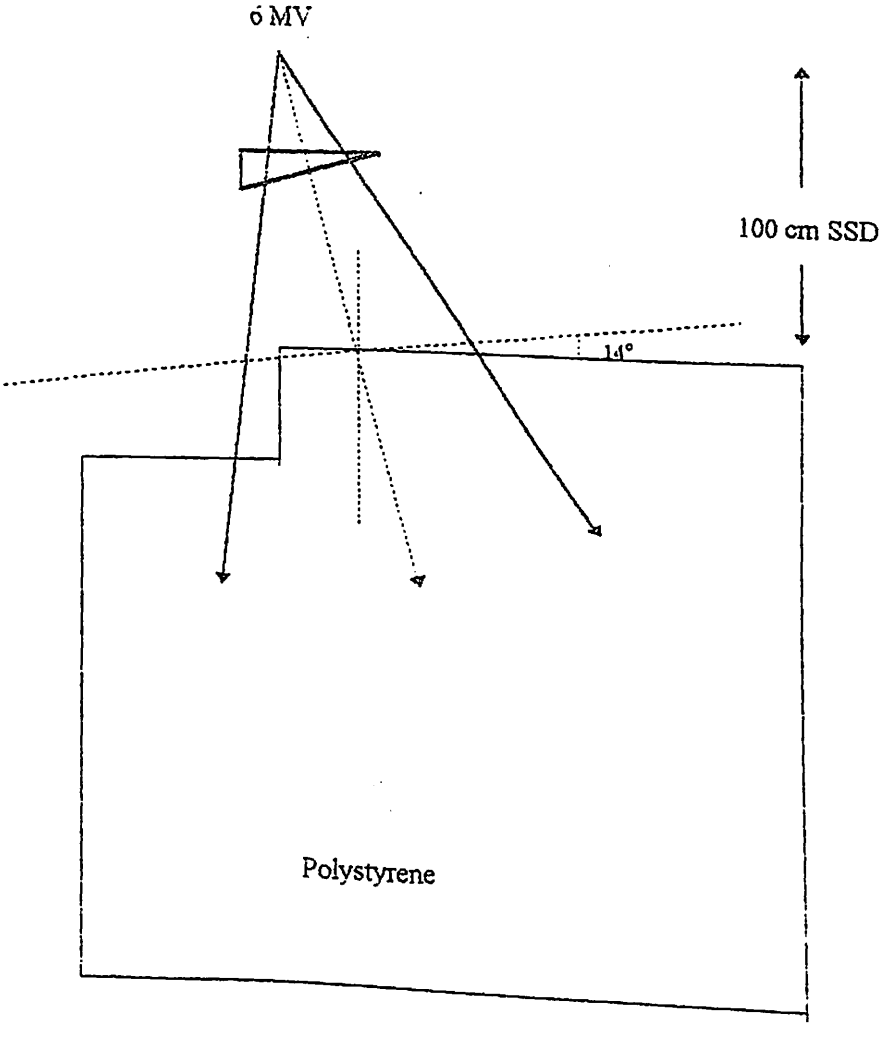

Figure 8. Set up of experiment 4

Figure 9c. Computed isodose lines in Y = - 3.0 plane in polystyrene phantom including point C in experiment 4.

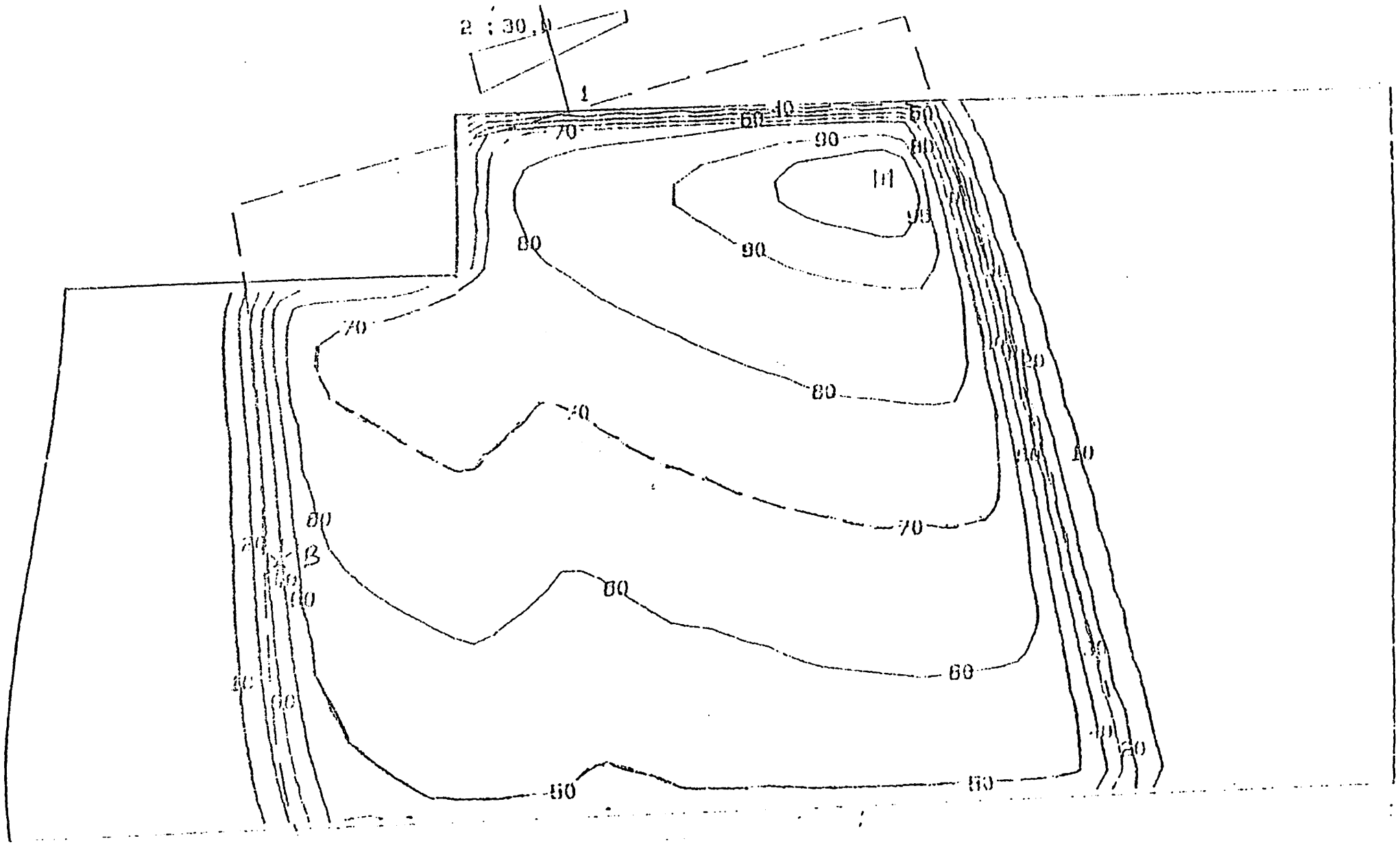

Figure 9b. Computed isodose lines in Y = - 1.5 plane in polystyrene phantom including point B in experiment 4.

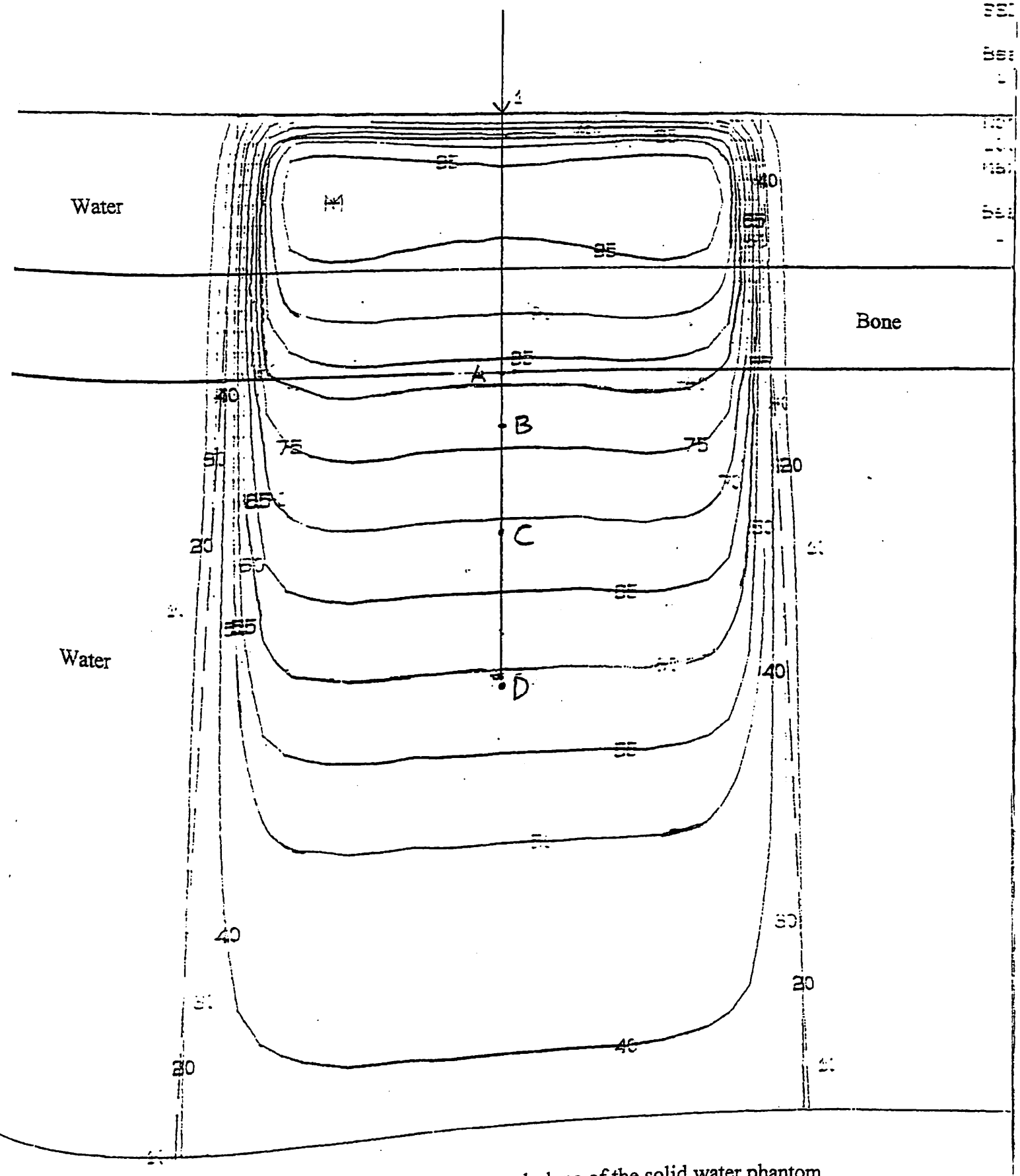

Figure 11. Calculated isodose lines in the central plane of the solid water phantom containing bone inhomogeneity. A, B, C and D are the measurement points on the central axis in experiment 5.

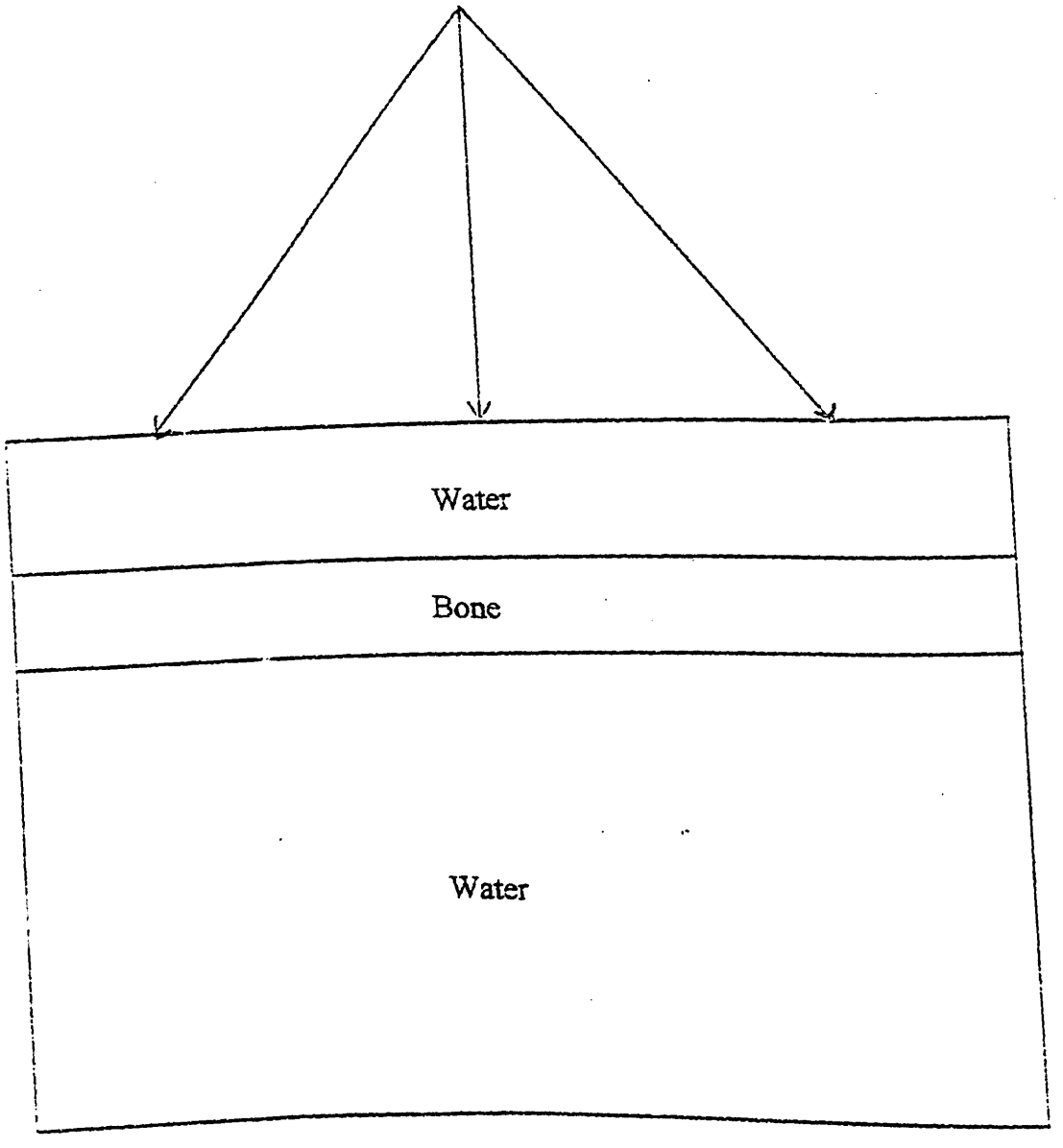

Figure 10. Set up of experiment 5

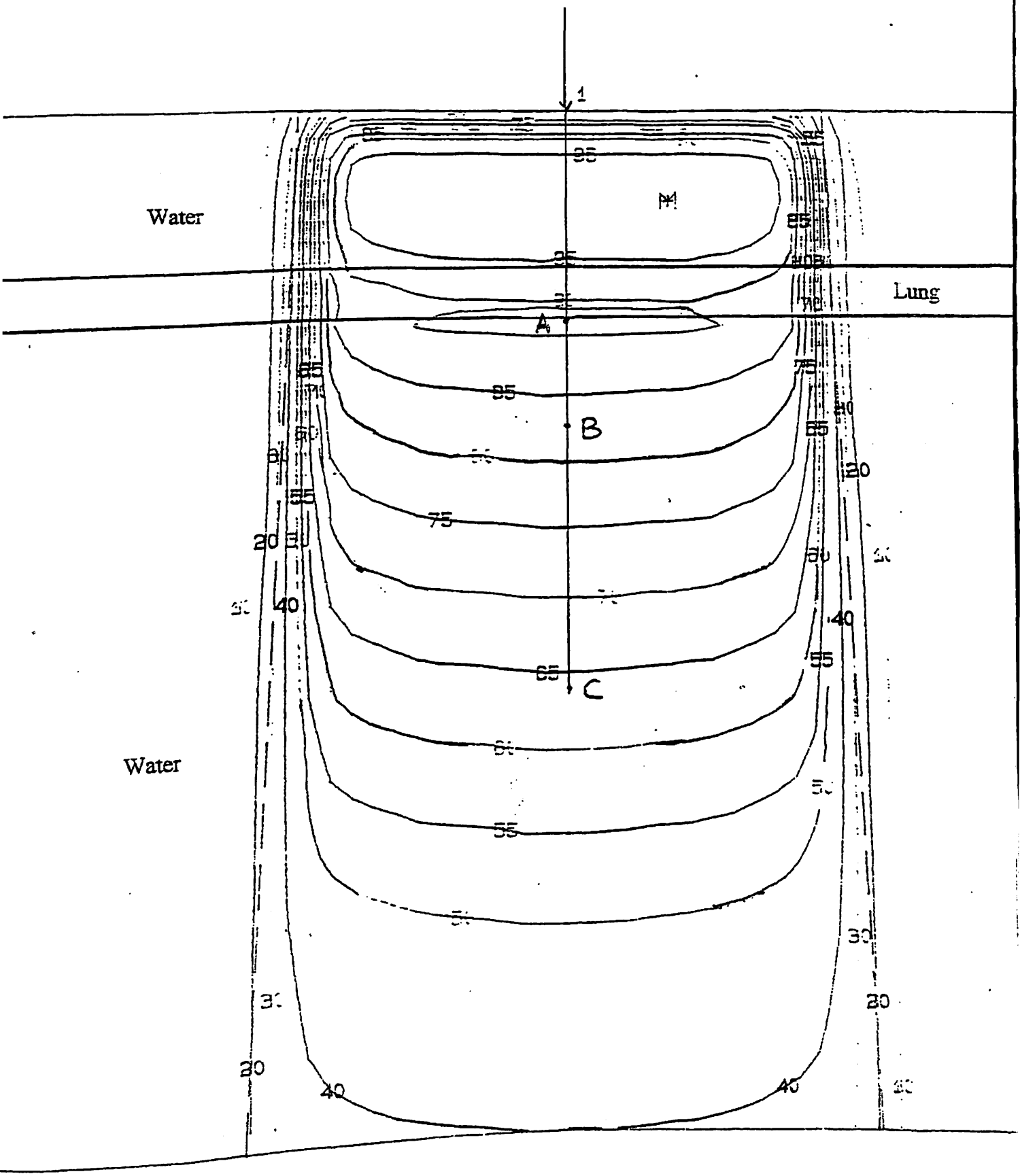

Figure 13. Calculated isodose lines in the central plane of the solid water phantom containing lung inhomogeneity. A, B and C are the measurement points on the central axis in experiment 6.