Nuclear Instruments and Methods 208 (1983) 677–683
North-Holland Publishing Company

APPLICATION OF SYNCHROTRON RADIATION TO THE STUDY OF MAN'S CIRCULATORY SYSTEM

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The selective X-ray imaging method of the patient's circulatory system at the absorption edges of elements, which uses synchrotron radiation, is considered. The first experimental results obtained at the Br and I K-absorption edges are presented. The advantages of the method described are analysed compared to the traditional X-ray imaging of the patient's blood vessels. Estimates for the limiting sensitivity of the method are given and the requirements on the apparatus and possible synchrotron radiation sources are considered. Problematic questions are discussed as well.

1. Introduction

The essential advantages of synchrotron radiation (SR) over the radiation of X-ray tubes together with the highly developed procedures of data acquisition, storage and displaying in a form convenient for a researcher, which are currently being used in elementary particle physics, enables one to raise the conventional methods of X-ray medical diagnostics to a qualitatively new level [1]. The present paper is devoted to the possibility of studying the pathology of the circulatory system and different organs in the human body that are capable of storing, in appreciable concentrations ($\gtrsim 0.1\%$), X-ray contrast compounds (for example iodine) by selective X-ray exposure at the absorption edges of elements.

A study of the pathology of the circulatory system is extremely informative from a medical point of view. This is the innate or acquired pathological changes in the circulatory system, which can reflect diseases or disorders of the internal organs.

At present, angiography methods – the radiographic study of blood vessels – are well-developed in medicine [2]. The main idea of angiography is to introduce a highly-concentrated contrast substance (with 30–50% of iodine in it) as close as possible to the point under study. The contrast substance, up to 60–80 ml, is injected into the point by means of a catheter inserted into one of the large blood vessels. After injection a fast exposure of a series of radiographs is carried out. In practice, the angiographic study is a specific surgical operation with a rather high degree of risk performed under X-ray monitoring.

The method described below makes it possible to avoid the surgical injection of a contrast substance into the region under examination and requires only a low mean concentration ($\lesssim 1\%$) of the substance in the blood. Such a concentration can be obtained, for example, by injecting a contrast substance into the vein regardless of the location to be examined.

2. The main principles and possibilities of the method

It is well known that the dependence of the X-ray absorption coefficient μ on radiation wavelength at definite wavlengths changes discontinuously – there are "jumps" at the absorption edges (fig. 1). The greatest

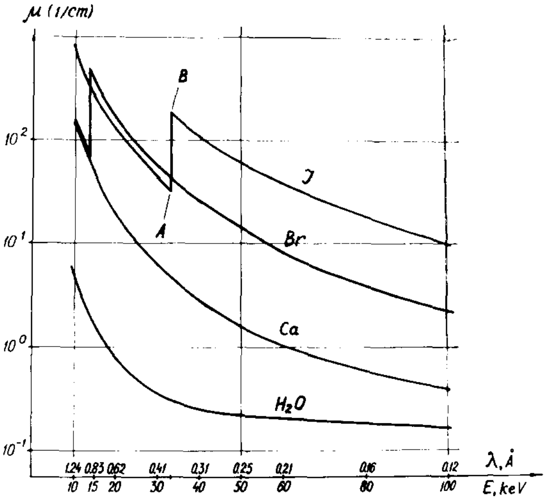

Fig. 1. Dependence of the linear X-ray absorption coefficient on wavelength (energy of X-ray quanta) for some substances.

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jump occurs at the K-absorption edge. Separation of the high-intensity radiation of a definite wavelength from the SR beam by means of a monochromator permits X-ray patterns to be selectively exposed below (point A in fig. 1) and above (point B), the K-absorption edge of the element under study. When the radiation passes through the part of the body containing this element, the intensity of the transmitted radiation decreases drastically due to the jump-like change of μ at the absorption edge if the wavelength is switched on from point A to point B. During the wavelength change from point A to point B, the change of X-ray absorption in the remaining chemical components of the body is insignificant. In view of this, the difference picture (obtained by subtracting the radiograph taken above the K-absorption edge from that taken below the edge) contains information only on the distribution of the element in question. If I_A and I_B are the intensities of the radiation transmitted through the body at some point in the image at wavelengths λ_A and λ_B respectively, then the quantity

$$\xi = \ln\left(\frac{I_A}{I_B}\right) = \ln\left(\frac{I_B+\Delta I}{I_B}\right) \simeq \frac{\Delta I}{I_B} \simeq c\cdot d\cdot\rho\cdot\Delta\mu \qquad (1)$$

is proportional to $c\cdot d$ of the element under study, where: c is the concentration, ρ is the blood density, d is the blood vessel diameter, $\Delta\mu = \mu_B - \mu_A$ is the difference between the mass coefficient at the absorption edge. With the use of X-ray selective imaging, a significantly higher effective sensitivity to the concentrations being detected can be expected over the existing angiography methods.

With low concentrations of the element under study the decrease in the intensity of the transmitted beam at the K-edge becomes comparable with increasing the intensity due to a monotonic decrease of the absorption coefficient μ_0 of the body (the object). This effect limits the ultimately detectable concentrations c^*, because the exact dependence $\mu_0(\lambda)$ in the human body is unknown. This limitation can be significantly improved by additional X-ray exposure at a third wavelength $\lambda_C = \lambda_A + \Delta\lambda$, where $\Delta\lambda = \lambda_A - \lambda_B$. In this case, the quantity proportional to concentration will be

$$\xi = \ln\left[I_A^2/(I_B\cdot I_C)\right] \qquad (2)$$

instead of (1).

The main limiting factor in radiation exposure with three wavelengths is the permissible adsorbed dose delivered to the patient during examination, and hence the finite statistics of detected quanta. The ultimately detectable concentration due to the latter effect may be estimated as follows:

$$c^*\cdot d = 6\times10^{-5}\left[\frac{\mu_0}{D\lambda}\right]^{1/2}\frac{\exp(0.5\mu_0\rho_0 A)}{b\rho\Delta\mu}. \qquad (3)$$

Here A is the body thickness in cm; ρ_0 is the mean density of the body in g/cm^3; D is the total absorbed dose (for three radiographs) on the surface of the part

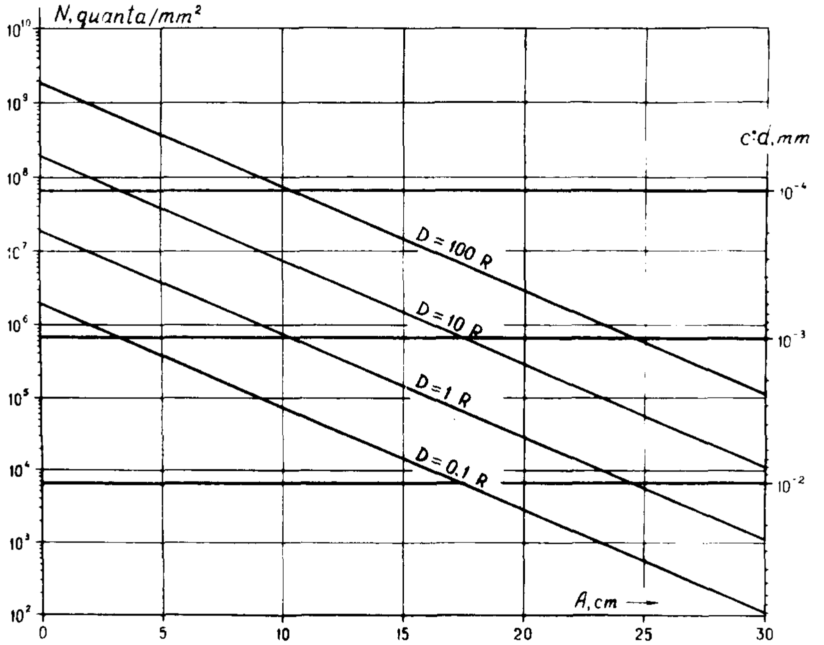

Fig. 2. Number of quanta N (left coordinate axis) per point of one image, which passed through a body part of thickness A at different total doses of irradiation D. The level of the products (right coordinate axis) of the ultimately detectable iodine concentration c^* in the blood vessels under examination of diameter d.

of the human body under irradiation, in R; b is the spatial resolution of the radiograph in cm; d is in cm; λ in Å; μ_0 and $\Delta\mu$ in cm^2/g; ρ in g/cm^3.

To examine different organs of the human body, it is necessary to use hard X-ray radiation with a quantum energy of $\gtrsim 30$ keV. Let us evaluate the possibilities of the method for studying the patient's blood system at the I K-absorption edge ($\lambda = 0.3739$ Å; $\Delta\mu = 30.1$ cm^2/g; $\mu_0 = 0.325$ cm^2/g; $\rho_0 \simeq \rho \simeq 1$ g/cm^3) with the help of X-ray exposures at three wavelengths. The spatial resolution of the radiographs is taken to be equal to 1×1 mm^2. In this case, the ultimately detectable concentrations of iodine in the blood versus the thickness A of the part of the body under examination, the total dose of irradiation on the body's surface and the diameter of the blood vessels under study can be estimated with the help of fig.2. If the number of quanta N is larger than a definite level $c^* \cdot d$, this implies the possibility of detecting a concentration c^* in blood vessels of diameter d.

The reference data [3] on the radiation sensitivity of different human organs show that in practice, the absorbed 20 R dose does not lead to their visible alteration. If the dose, $D = 20$ R, is taken as a permissible one, then in studying the thorax ($A \simeq 25$ cm) we have $c^* \cdot d = 2.4 \times 10^{-3}$ mm. Thus, for a 1 mm vessel diameter an iodine concentration $c^* = 2.4 \times 10^{-3}$ can be expected to be detected. For vessels of 5 mm diameter the detectable concentration will be $c^* = 4.8 \times 10^{-4}$, respectively. In studying the thinner parts of the body the quantity c^* decreases significantly. Without going into details of injecting the maximum possible concentrations of iodine into the blood, we would like to point out that, according to conventional angiography methods, up to 80 ml of the highly-concentrated contrast substance is introduced ($\simeq 50\%$ iodine). This corresponds to a mean concentration of I in the blood of about 8×10^{-3}, which appreciably exceeds the above estimates.

It is worth noting also that it is necessary to synchronize the radiation exposure with different phases of breathing and cardiac contractions, and hence to study the heart and large blood vessels at different stages of blood filling.

Thus the estimates presented above show that one can hope to detect, by the method described, blood vessels of $\gtrsim 1$ mm diameter in the chest region at reasonable doses of radiation.

3. Experimental results

At the beginning of our work, in the Autumn, 1979, we had no SR source which could produce an intense X-ray beam of 33.2 keV quanta energy. Therefore, the method was tested at the storage ring VEPP-3 [4] near the Br K-absorption edge using synchrotron radiation from the bending magnet and X-ray pictures taken at two wavelengths. The experimental scheme is shown in fig.3. The SR beam monochromatized by a crystal was passed through a hole in the shielding screen and then through the object located on a table with two-coordinate displacement. Finally, it was detected by the ionization chamber. The radiation wavelength needed was chosen by the crystal precision-rotation system. During the exposure the object was scanned in two coordinates relative to the hole. The picture detected consisted of 100×100 points; the intensity was measured for two wavelengths at each point of scanning. The experiment was completely automatized with the help of the ODRA-1325 computer.

The first experimental results were obtained in December of 1979. The experiments at the Br K-absorption edge carried out with the test samples (see fig. 4) have demonstrated the possibility of detecting a Br concentration of $\sim 10^{-3}$. This value coincides well with the calculated estimates.

One of the objects examined at the Br K-absorption edge was a part of the helix of a live rabbit. The Br concentration in the rabbit's blood was artificially created by fractional injection of potassium bromide solution through a catheter into the vein of a hindleg; the rabbit was intravenously narcotized. 14 ml of the 10% KBr solution was introduced; the estimated Br concentration in the rabbit's blood was 2×10^{-3}. The sections for exposure were chosen to be 10×10 mm^2 in size and the spatial resolution was 0.1×0.1 mm^2. Fig.5 demonstrates the usual (for one λ) and difference (the distribution of ξ) pictures of the section chosen. Two blood vessels are clearly observed in the upper and middle parts of the difference picture. In the lower part of the picture a wide bed with indistinct space boundaries is observed that looks very much like a branched small capillary network. In the usual picture only the collagenic increased thickness in the helix (near the upper vessel in the difference picture) is well seen; the blood vessels are practically not observed.

The results obtained at that time were reported at the Conference on Utilization of Synchrotron Radiation SR-80 (Novosibirsk, October 8–10, 1980) and at the third Soviet–England Seminar on Synchrotron Radiation (Moscow, April 6–8, 1981) and were also published in ref. 5.

After the superconducting snake, located in the straight section of the storage ring VEPP-3 [6,7] had been employed as a powerful generator of SR, it became possible to work at the I K-absorption edge. In the summer of 1981, a series of experiments was carried out at an energy of 33.2 keV using synchrotron radiation from the snake. Much attention, at this time, was paid to the testing of the monochromator construction and to the choice of suitable crystal-monochromators in

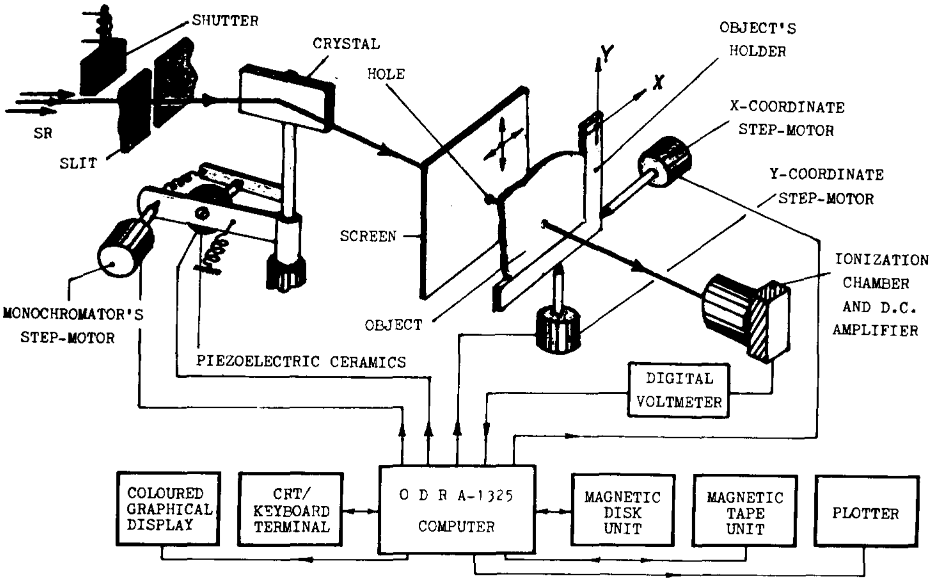

Fig. 3. Schematic of experimental setup for radiation exposure at the X-ray absorption edges of elements under study.

order to separate quanta of the given energy. As a result, the two-crystal monochromator with parallel Ge(422) crystals was chosen and tested. The monochromator ensured that the radiation beam had 40 × 1 mm^2 in size and a degree of monochromaticity of $\Delta\lambda/\lambda = 1.2 \times 10^{-3}$. The maximum horizontal size of the beam was determined by the extraction channel for SR from the snake, and the sizes of crystals permitted one to acquire a monochromatic beam of up to 100 mm horizontal width.

In addition, measurements were made of the range of detectable concentrations of iodine in solution. The thickness of the solutions along the beam path was 1 g/cm^2. Measurements were made by taking absorption spectra of solutions in the vicinity of the I K-absorption edge. Fig.6 illustrates the absorption spectra of solu-

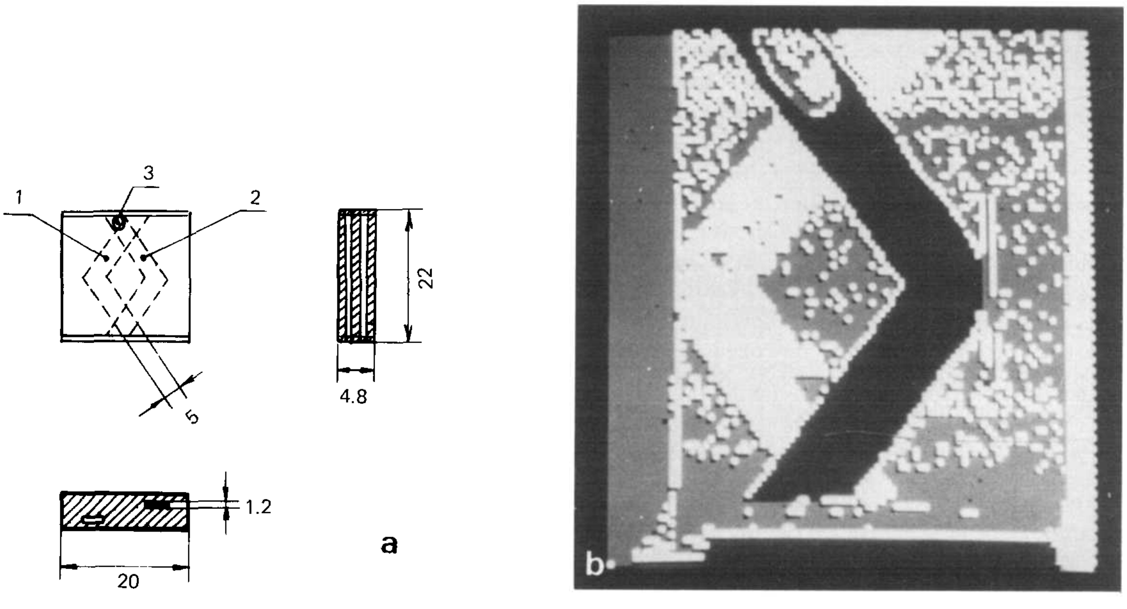

Fig. 4. Scheme (a) and a difference picture (b) of a test sample. Channels 1 and 2 in plexiglass are filled with Br solutions with 10^{-3} and 10^{-2} concentrations, respectively; 3 – air bubble in channel 2.

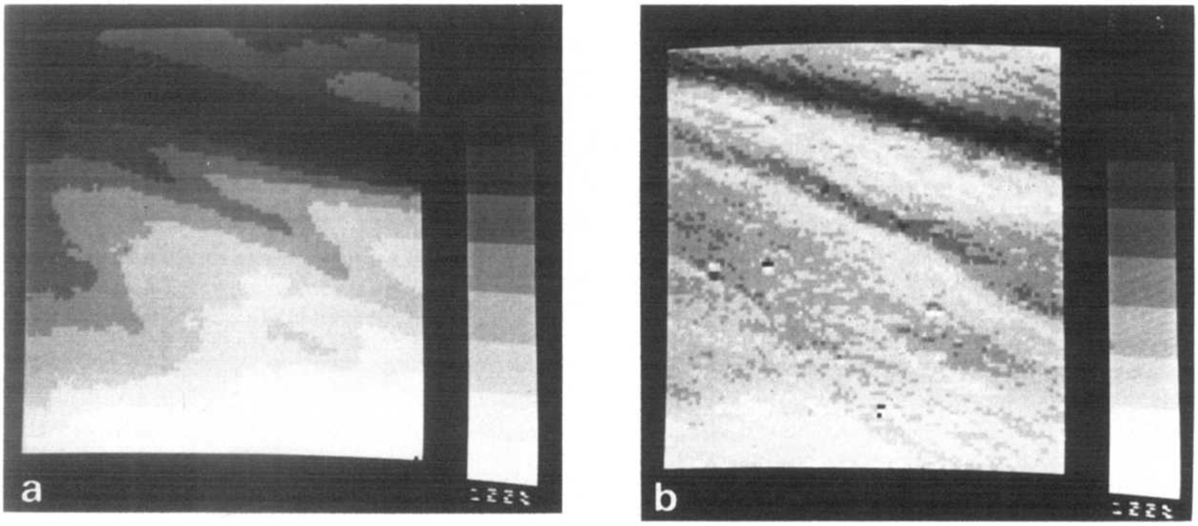

Fig. 5. Conventional (a) and difference (b) pictures of a part of the rabbit's helix taken at the Br K-absorption edge.

tions with different concentration of iodine. The signal from the ionization chamber is plotted along the y-axis in relative units. The negative slope of the curves in the region of the smooth variation of the absorption coefficient corresponds to an exponential decrease in intensity of the SR from the snake with increasing quanta energy. Analysis of the curves shows that an iodine concentration of 10^{-3} is at the limit of detection and is in agreement with the calculated value of c^*.

It is worth noting that in all the experiments the values of limiting concentrations were determined by a smooth variation of the absorption coefficient of objects with transition from λ_A to λ_B rather than by the statistics of the quanta. No measurements at three wavelengths have been performed.

The first experimental results obtained at the K-absorption edges of Br and I have demonstrated good agreement between the measured limiting concentrations and the expected ones. Moreover, these results have indicated our understanding of the possibilities of the method is correct. However, in order to obtain difference pictures for exposure times of the order of a

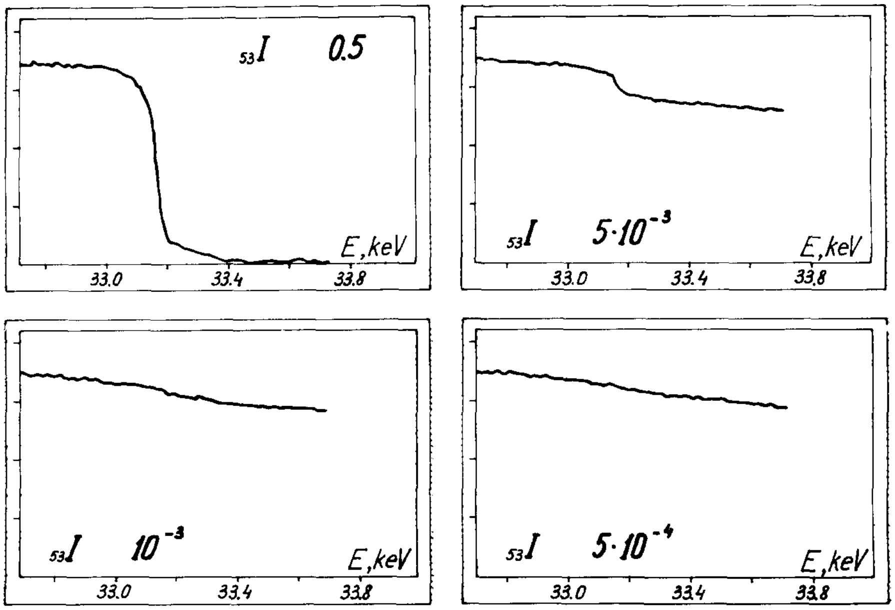

Fig. 6. Absorption spectra of solutions at different concentrations of iodine.

few minutes or less (in our experiments recording of one difference picture at two wavelengths took 1.5 h), it was necessary to design suitable equipment.

4. Requirements for experimental equipment

It seems useful to formulate the medical requirements for the parameters of a future medical station. Apparently, doses of radiation within 0.1–20 R should be regarded as reasonable for the human body. The actual value will be determined by the location under examination and the aim of the diagnostics. The characteristic size of an area of interest for examination is of about 10×10 cm^2. The spatial resolution of radiographs, as has been shown above, can reach a value of about 1×1 mm^2. One of the requirements is the possibility of recording the difference radiographs at different phases of the systole cycle. The time necessary to take one difference picture should not exceed reasonable limits of the order of few minutes or less.

At present, the use of a one-coordinate detector and line-by-line taking of radiographs seem to be most practical. Below the requirements for the basic elements of a medical station – monochromator and detector – are formulated.

4.1. Monochromator

The effective width of the K-absorption edge of iodine is $\Delta\lambda/\lambda = 5 \times 10^{-3}$. In view of this, in order to detect as small a iodine concentration as possible, a monochromator should provide an X-ray beam monochromaticity of $\Delta\lambda/\lambda \lesssim 10^{-3}$. The beam sizes at the monochromator exit should be of the order of 100×1 mm^2.

4.2. Detector

A one-coordinate detector should have a spatial resolution of $\lesssim 1$ mm and a sensitive region size of about 100 mm. It is clear that the obligatory requirement of the detector is a high detection efficiency (close to 100%) for 33.2 keV quanta. The possibility of synchronizing detector operation with systoles means that the time of radiation detection in one line, τ, should be much less than that of the heart cycle (~ 1 s), i.e. $\tau \lesssim 0.1$ s. With such a value of τ the total time for recording a difference radiograph consisting of 100×100 points at three wavelengths will be about 30 s for exposure without synchronization with the cycle of systoles and $\lesssim 5$ min for exposure with synchronization. The accuracy of the intensity measurement by each detector channel should not be less than the statistical spread of the number of quanta in the channel. For the possibility of recording radiographs of different parts of the human body at different irradiation doses, it is desirable that the dynamical range of the detector be sufficiently large, of the order of $\gtrsim 10^3$. Table 1 gives an idea of some of the requirements for a detector to observe blood vessels of 1 mm diameter at different irradiation doses.

Taking into account the requirements listed in table 1 and the possibilities of SR sources which are available at the Institute of Nuclear Physics, the use of a detector in the counting mode seems to be the most reasonable option.

5. Conclusion

At present, in the USSR, there are two SR sources at which work dealing with the selective recording of radiographs at the K-absorption edge of iodine can be performed. These are the superconducting snake, installed at the storage ring VEPP-3 [6,7], and the storage ring VEPP-4 [4]. The main parameters of these sources are listed in table 2.

At a distance of 20 m from the point of radiation, the fluxes of quanta per unit area, at a 33.2 keV quanta energy, are quite sufficient, in practice, for the selective recording of radiographs without focusing the SR beams.

At the present time, the main effort for developing the method is being devoted to the development of an adequate one-coordinate detector.

Table 1

Total dose of irradiation (for three radiographs), [R]	Ultimately detectable concentration of iodine in the blood	Number of quanta on the surface of the part under study (for one radiograph), [quanta/mm^2]	Number of quanta on detector after passing through a 25 cm body thickness (for one radiograph), [quanta/mm^2]	Counting rate of detector, [quanta/s/mm^2]	Necessary accuracy of measurements
20	2.4×10^{-3}	3.8×10^8	1.1×10^5	$\gtrsim 1.1 \times 10^6$	$\lesssim 3.0 \times 10^{-3}$
1	1.1×10^{-2}	1.9×10^7	5.7×10^3	$\gtrsim 5.7 \times 10^4$	$\lesssim 1.3 \times 10^{-2}$
0.1	3.4×10^{-2}	1.9×10^6	5.7×10^2	$\gtrsim 5.7 \times 10^3$	$\lesssim 4.2 \times 10^{-2}$

Table 2

SR source	Electron energy in storage ring [GeV]	Electron current in storage ring [mA]	Magnetic field at the point of radiation [kG]	Critical wavelength of radiation [Å]	$\dot{N}\left(\frac{\text{quanta}}{\text{s}\cdot\text{mm}^2}\right)$ $L = 20$ m, $\Delta\lambda/\lambda = 10^{-3}$, $\lambda = 0.3739$ Å
Superconduct. snake at VEPP-3	2.0	50	33	1.41	4.0×10^{10}
VEPP-4	5.5	10	10	0.62	1.2×10^{10}

It is necessary to mention the difficulties which are likely to be encountered in the selective X-ray exposure of parts of the human body. First, a large number of capillaries on the path of the X-ray beam can weaken the contrast of the blood vessels under study. Second, detection of all blood vessels in the region under investigation (unlike conventional angiography where only the vessels being analysed are contrasted) can significantly complicate the picture under observation. If the image is too complicated for its clear interpretation, then the particular part of the body should be exposed in several projections and the difference pictures should be additionally analysed. An experimental study needs to be done to resolve these questions.

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