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MEDICAL APPLICATIONS OF SYNCHROTRON RADIATION*

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ABSTRACT

Ever since the first diagnostic x-ray was done in the United States on February 3, 1896, the application of ionizing radiation to the field of medicine has become increasingly important. Both in clinical medicine and basic research the use of x-rays for diagnostic imaging and radiotherapy is now widespread. Radiography, angiography, CAT and PETT scanning, mammography, and nuclear medicine are all examples of technologies developed to image the human anatomy. In therapeutic applications, both external and internal sources of radiation are applied to the battle against cancer. The development of dedicated synchrotron radiation sources has allowed exciting advances to take place in many of these applications. The new sources provide tunable, high-intensity monochromatic beams over a wide range of energies which can be tailored to specific programmatic needs. This paper surveys those areas of medical research in which synchrotron radiation facilities are actively involved.

DISCLAIMER

1. Introduction

The field of medical applications of ionizing radiation, like all of x-ray physics, got its start on November 8, 1895 when Wilhelm Konrad Roentgen discovered x-rays [1]. The wonderful x-ray of his wife's hand with her ring clearly defined created a tremendous level of excitement in the scientific community. In the context of this paper on medical applications, it is interesting to note that that x-ray showed the ability to distinguish underlying skeletal structures from the soft tissue around it. Within weeks, laboratories throughout the world were studying the applications of the new wonder rays. One of the amazing things is the extraordinary rapidity with which the news spread without the use of FAX machines or electronic mail! Indeed, the general public instantly became aware of the discovery and reacted with great hysteria; e.g. the introduction of lead underware for demure individuals!

The news of the discovery almost immediately crossed the Atlantic and the United States' laboratories were no less fascinated than their European counterparts. The medical profession reacted swiftly to the possibility of using the rays as a diagnostic tool, and on February 3, 1896 (less than three months after Roentgen's discovery) the first medical diagnostic x-ray in the United States was taken by Dr. Gilman Frost of the Dartmouth Medical School.

In some ways, the synchrotron x-ray community finds itself in a similar situation. A new, powerful tool has been developed over the past several decades, it is in use around the world, and scientists from all disciplines, including medicine, are eager to develop applications for it. Of course, no one believes that anything can happen in less than three months anymore. The world has learned about safety (soon after the use of the first x-ray tubes, mysterious red rashes started showing up on some individuals!), the machines are enormously complex and they are expensive. Nevertheless, the utilization of synchrotron radiation facilities for medical purposes is just one of the latest in a long, successful line of advances in technology which started only 100 years ago in the small laboratory in Würtzburg, Germany. Today, health care in some ways is dominated by technology, examples being the use of both internal and external sources of x-rays for radiotherapy, imaging using x-rays, ultrasound, and magnetic resonance, and a myriad of electronic marvels.

In order to understand the role that the synchrotron will have in the overall health care field, a survey of the existing imaging and radiotherapy technologies in use at present day medical facilities was recently completed [2]. Although limited in scope, this survey has proven useful in thinking about the future. The results of the effort are condensed and summarized in Table 1. This table presents the most commonly used medical imaging and therapeutic modalities which utilize ionizing radiation, as well as two which are commonly used now which do not. They are shown for completeness since they indeed compete with x-ray based imaging, and they present less risk to the patients. The scope of this paper does not allow a discussion or comparison of all of these modalities. In fact, the discussion will be limited to those areas where the two fields of medicine and synchrotron radiation science have joined to create new tools for medical research, diagnosis, and treatment. In some cases, examples are given in an attempt to show the widespread use of the synchrotron in medicine. The references cited are meant to be guides to those facilities and scientists working in a specific area and certainly are not exhaustive.

2. Properties of synchrotron radiation

2.1 Advantages

The advent of dedicated synchrotron facilities made possible the long term planning for the utilization of the x-ray and ultra-violet beams in medical research programs. The overriding features of the synchrotron beams which make them applicable to medical research are their extremly high intensity and broad-band energy spectrum. As an example, fig. 1 shows the x-ray spectrum from the X17 superconducting wiggler beamport at the National Synchrotron Light Source (NSLS) [3] compared with a high power conventional tube source. Several orders of magnitude separate the two spectra and the smooth, continuous spectrum from the synchrotron contrasts with the sharply peaked characteristic emission peaks from the tube. The advantages of the synchrotron arise mainly from these two features and are summarized in Table 2. Basically, the high intensity and tunability allow monochromatic beams to be generated at virtually any energy. The standard problem of beam hardening in both medical imaging and therapy is eliminated by the monochromatic beams since the energy spectrum does not change

with passage through tissue, only the intensity changes. The tunable spectrum allows enhancement of images and therapeutic dose by selection of the most effective energy for a given procedure. Examples will be given later of the use of K-absorption edge enhancement for imaging and radiotherapy. Benefits to the patients, important considerations in human applications, come from more effective dose delivery in therapeutic modalities and less dose with greater image quality in imaging procedures.

Along with the high intensity and tunability, there are several other advantageous properties of the synchrotron which are sometimes utilized in the research programs. The beams are very highly collimated in the vertical direction and are thus ideal for basic research programs such as protein crystallography and small angle scattering. This geometry is also perfect for the cerebral multiple energy computed tomography program to be discussed later. The radiation is emitted in very short pulses, with a well defined time between pulses. Some research programs have started to use this feature in doing real-time molecular dynamics and structural studies. The radiation is also plane polarized in the plane of the storage rings where the radiation is produced. This feature is exploited by researchers studying the helicity of DNA, for example, with a technique known as circular dichroism.

2.2   D sadvantages

Along with the advantages of the synchrotrons and their powerful beams come some distinct disadvantages for medical applications. These are noted in Table 2 and are important for both technical and sociological reasons. The planar beam geometry, mentioned above as an advantage in some programs, is a distinct disadvantage when one tries to create a large two-dimensional image. That is precisely the problem in the human coronary angiography projects to be discussed later. However, in the basic research areas, there are few such disadvantages. The real problem comes when considering the application of synchrotrons to clinical diagnostic programs for humans or even large scale research programs involving human subjects. At present, and in the foreseeable future, there is exceedingly little access to the synchrotron beams for medical purposes, due both to lack of development of such programs and the very high cost of both facilities and research beamlines. Assuming that technical matters can

be solved, it will be imperative to develop compact, high-energy spectrum sources which will be cost effective for hospitals, research centers, or medical centers [4]. Without such development, the medical applications will be limited to a few well defined research programs.

The short term future is clearly along the lines of basic research in which drug development may take place, new radiotherapy techniques may be developed and tested, and advanced imaging systems may become successful. These will all certainly happen on today's first and second generation sources and tomorrow's third generation sources. Whether or not any programs reach the level of clinical diagnostic or treatment centers will depend on the success of the present research programs, the acceptance of these technologies by the medical community, and the development of new compact sources.

3.   **Medical research at synchrotron facilities**

3.1   Overview

In the short time that synchrotrons have been available to the scientific community for x-ray and VUV science, they have been used in virtually all areas of medicine which use ionizing radiation. The research has not been confined to any one facility, but is being carried out throughout the world. The following examples will be accompanied by sufficient references to indicate where particular classes of research are being done.

A summary of most of the current research areas which involve synchrotrons is given in Table 3. Quickly surveying the table, it is obvious that the research already covers all dimension scales from the atomic and molecular level (EXAFS and structural biology), up through DNA (photon activation therapy and structural biology), chromosomes and cells (x-ray microscope), to tissues and organs (angiography and computed tomography). The applications are directed at many of the most difficult and important medical problems facing the human race. The research, as will be seen in detail later, is directed at brain and breast cancer imaging and therapy, development of new drugs, evaluation of cellular function, and coronary artery imaging in a manner which is safer for the patient than conventional means. All of the research programs involve some in-vitro research. In some cases like structural biology and

EXAFS (Extended X-ray Absorption Fine Structure), in-vitro research will be the only case due to the basic research nature of the subject matter. For that reason this paper will not discuss these very important, widespread technologies any further. However, references are included for structural biology [5] and EXAFS [6] which are good reviews of the subjects as they pertain to basic biomedical research. All of the other research projects have potential either for direct human subject involvement with the synchrotron x-ray beams (coronary angiography, mammography, computed tomography, and radiotherapy) or indirect through the development of radiation dose enhancement drugs (photon activation therapy). The x-ray microscope, although unlikely to be applied in-vivo to humans, may involve animal studies in the future. Only the coronary angiography programs at the NSLS and HASYLAB presently involve in-vivo human studies. Some early radiotherapy work at the NSLS has proceeded to the animal model stage. It is expected that within a few years, additional radiotherapy, mammography, angiography, and cerebral computed tomography programs will reach the in-vivo human studies level.

Before moving on to some of the major applications, it is necessary to mention one of the most recent advances in the use of synchrotron radiation. For many years, researchers have discussed the possible use of the intense, monochromatic x-rays in the range 10 - 30 keV for enhanced contrast in the images of breast tumors. The enhancement over present radiation sources comes from better spatial resolution and greatly enhanced tissue differentiation (dense tumor mass vs. surrounding soft tissue) due to the monochromaticity of the beams. The first efforts to study this problem have been reported by a group at the Laboratori Nationali di Frascati [7]. They have compared the radiography of excised breast tumors taken with conventional sources with those taken with monochromatic synchrotron beams and have reported higher contrast and better resolution. This work is in its very early stages. Workers from Vanderbilt University have also started to study the tissue differentiation of breast tumor using the NSLS [8]. This promises to be a very important area of biomedical research.

3.2   *Photon activation therapy*

Photon Activation Therapy (PAT) is a system being investigated as a therapeutic modality for the treatment of malignancies, particularly the highly lethal and malignant brain tumor,

glioblastoma multiforme. The PAT process involves the incorporation of a target atom in the immediate vicinity of a cell's critical site (DNA), followed by the activation of this atom with photons of energies suitable for the induction of the photoelectric effect and its concomitant Auger cascades. The Auger electrons impart significant damage at the critical site. In 1977 it was postulated [9] that through the use of stable halogenated pyrimidines incorporated in cellular DNA, followed by their activation with monochromatic photons above the K-absorption edge of the halogen, the photoelectric absorption would lead to the release of Auger electrons, contributing additional ionization within the DNA. The effectiveness of PAT for radiotherapy lies in the fact that the malignant cell pools are rapidly dividing relative to the normal tissue cells. It is therefore possible to incorporate stable halogens such as bromine or iodine into the cellular DNA. Radiation would then preferentially damage the malignant cells since they have incorporated the halogen.

Several investigators have attempted to demonstrate the increased effectiveness of x-rays attributable to the Auger effect. Some of the work has been done at synchrotron facilities. Among these are Shinohara [10] at the Photon Factory, Larson [11] at SSRL, and Menke [12] at HASYLAB. They all used BrdUrd (5-bromo-2'-deoxyuridine) as an analog of thymidine in the cellular DNA. All of the results failed to show any substantial enhanced sensitivity due to Auger processes resulting from the photoelectric absorption of photons above the K-edge of bromine. Recent work at the NSLS has confirmed the absence of measureable effects with BrdUrd using Chinese hamster V-79 cells [13].

However, there has now been some work reported in which iodine has been incorporated into the DNA of V-79 Chinese hamster cells [14]. The iodine was in the form of stable I-127 in the halogenated pyrimidine 5-iodo-2'-deoxyuridine (IdUrd) and was incorporated into the cellular DNA during cell replication as an analog of the natural base thymidine. The target atom was the iodine and the experiments used monochromatic photons above the K absorption edge at 33.17 keV. Although IdUrd is a known cell sensitizing agent, those experiments were designed to separate out the effects due to the Auger effect. The experiment was done at the NSLS using the X17 superconducting wiggler beamline [3]. Monochromatic photons above (33.4 keV) and below (32.9 keV) the iodine K-edge were used to determine if any additional biological damage would accrue from the Auger cascades. The 33.4 keV photons were found

to be a factor of 1.4 times more effective in increasing the severity of damage to the iodinated cells than were the 32.9 keV photons. These results, the first demonstration of the effectiveness of Auger electrons in enhancing the effects of radiation, are shown in fig. 2. In this experiment there was a 16.3% replacement of thymidine by the IdUrd. The total therapeutic gain (relative to the non-iodinated controls) was a factor of 3.1, close to the predicted value [15]. PAT has been described as a potential clinical modality for the treatment of malignant brain tumors [16]. Samarium-145, which emits 40 keV photons, has been identified as a radioisotope which is nearly ideal for PAT with iodine. Implantation of Sm-145 brachytherapy sources can be used for delivering radiation locally.

3.3   Radiotherapy

Radiotherapy is that process whereby a large dose of ionizing radiation in the form of gamma-rays, x-rays, or particle beams is targeted onto a tumor or malignant cells in order to kill the cells. The dose can be delivered by external beams created by x-ray machines or from the decay of radioactive sources such as Co-60. The dose can also be delivered by use of radioisotopes such as I-125 or Cs-137 which are delivered into the body to the tumor site or encapsulated and inserted into the region of the tumor. The main problem associated with all of these forms of therapy, although sometimes effective in killing the malignant cells, is the attendant high radiation dose to the normal tissue which is in the region of the tumor or, in the case of external beam therapy, between the external body surfaces and the deeply buried tumor.

One of the most effective means of increasing the dose to the tumor and sparing intervening normal tissue is to use stereotactic radiosurgery [17]. In that procedure one or more highly collimated radiation beams is directed at the tumor while the patient is rotated or the beams are fired from varying directions. The crossing point of the beams is at the target tumor, thereby delivering a dose equal to the sum of all the beams to the target and delivering a fraction to all other tissue.

The development of the high energy synchrotron beams has given rise to many ideas which are directed at increasing the effectiveness of x-ray dose to tumors and decreasing dose to normal tissues. The discussion above of photon activation therapy is one way of increasing

the effective dose to the malignant cells since they preferentially incorporate the halogen in the DNA relative to the non-proliferating normal cells. Coupling that to the ability to tune the highly monochromatic synchrotron radiation beams (which are inherently collimated) to the relevant K-edge should provide a very efficient tool for some forms of external beam therapy.

The monochromatic synchrotron radiation beams can be very highly collimated in either planar or cylindrical beam geometries and can be either focusing or non-focusing. With the development of high energy sources it is now possible to have beams with energies in the range of 50 keV and above. These are excellent for targeting tumors deep in the brain. The geometry is ideal for stereotactic radiosurgery and the monochromatic beams will not beam harden. Hence, the radiation dose to the patient will be efficiently delivered. With the development of high Z elements which can be bound to tumors, the tunability of the source will allow selective targeting of the tumors. In a later section of this paper, a program on cerebral computed tomography will be discussed. It will be obvious that the same apparatus on the synchrotron beamline could be used to both position the patient and then deliver a carefully defined radiation dose to the tumors.

3.4   X-ray microscopy

The x-ray microscope has been developed to image, on a scale of microns or less, the elemental distribution in tissues and cells. The intent is to supplement existing technologies such as the electron or light microscopes and to open up new imaging potential where highly penetrating radiation is necessary. There are two distinct types of instruments, differentiated chiefly by the photon energy range over which they operate and, to some degree, the spatial resolution of the images.

The development of very high brightness synchrotron radiation sources (both bending magnet and more recently undulator sources) has led to major advances in soft x-ray microscopy (SXRM). The microscopes require the coherent flux and high intensity available from these sources. The first of the two types of microscope is the SXRM which uses x-rays in the wavelength range known as the water window. Between the carbon and oxygen K-edges (2.5 - 4 nm) water is relatively transparent. Thus, wet biological specimens can be imaged with high

contrast, especially in systems employing the technique of K-edge digital subtraction imaging.

There are a number of soft x-ray microscopes operating around the world. The present generation of microscopes has been constructed on undulator lines to take advantage of the extremely high brightness of the sources. Some of the instruments currently being operated are at Daresbury Laboratory [18], the Photon Factory [19], and the NSLS [20]. The microscope at the NSLS has several modes of operation. Besides the scanning transmission mode, it operates as a scanning photoemission microscope for ultrahigh vacuum (non-biological) studies and in a holographic mode. In the holographic mode, two-dimensional reconstructions at a resolution of 0.06 microns are possible. It may eventually be possible to image wet biological samples in three dimensions.

The scanning microscope is capable of imaging wet samples since the beam is focused by a zone plate and exits the vacuum through a very thin silicon nitride window. The sample is raster scanned through the beam to build up a two dimensional image. Presently the spatial resolution is about 0.06 microns. The monochromator selects the incident energy and, when desired, dual-energy imaging at an absorption edge is done. Fig. 3 is an image of a naturally occurring chromosomal aberration called a dicentric, isolated from the meristematic tissue of *Vicia faba* root tips [21]. The image was recorded with 50 nm pixels and 35.3 nm (350 eV) soft x-rays. The dose was 40 MRad to the wet sample.

In order to image dense, high Z materials or to study trace elements of high Z materials in a matrix such as bone, it is necessary to turn to the x-ray microscope (XRM). In the present context that means one which operates on a hard x-ray line at energies greater than about 3 keV. An example of such a beamline is one built at the NSLS [22]. Images can be produced by measurement of fluorescent x-rays or of the attenuation of the incident beam by the specimen. Maps of the elemental distributions or linear attenuation coefficients can be made by scanning of the specimen past the beam. Because of the higher energies of this instrument, computed microtomography can be used for nondestructive images through the specimen in either fluorescence emission or absorption mode. The NSLS XRM uses bending magnet radiation and can be operated in the white beam mode or with a premonochromator. Beam sizes at the sample are determined by slits and pinholes, with beam sizes of about 2 microns in standard use.

The study of the distribution of trace levels of therapeutic gallium in bone illustrates the application of the XRM to biological problems. Gallium nitrate inhibits calcium release from bone and has proven to decrease the resorption of bone associated with cancer. In a recent experiment the XRM was used to map the distribution of gallium in the bones of rats treated with gallium nitrate [23]. After short in-vivo administration of gallium nitrate, it was found that the gallium preferentially localized to the metabolically active regions of the bone, regions where new bone formation was ocurring. These studies represent a first step toward understanding the mechanism of the action of gallium in bone.

3.5 Multiple energy computed tomography

Monochromatic synchrotron x-rays have two distinct advantages over the wide-energy band bremsstrahlung radiation obtained from x-ray tubes for radiology in general and for computed tomography (CT) in particular. The monochromatic x-rays do not "beam harden", an effect in which the low energy end of the photon spectrum attenuates more than the high energy end. The average energy shifts to higher energy as a function of penetration into the body. This is particularly troublesome for image reconstruction of CT images. Second, the tunability of the spectrum allows both dual-photon absorptiometry (DPA) and K-edge subtraction (KES) imaging. A system called Multiple Energy Computed Tomography (MECT) has been developed at Brookhaven National Laboratory which will utilize synchrotron radiation beams for DPA and KES of the human cerebrum [24]. The system is being developed at the X17 beamport of the NSLS [3].

DPA is an imaging method in which the attenuation of x-rays at two greatly different energies (e.g. 40 and 100 keV) is measured to obtain two different images of the subject. One mainly represents the concentrations of low Z elements and the other mainly the intermediate Z elements. The DPA image of the low Z element group will emphasize concentrations of H, C, N, O, and Na while that of the intermediate Z group will emphasize P, S, Cl, K, Ca, and Fe. In particular, the second group includes the neurologically important elements K and Ca. Abnormal brain-tissue concentrations of these elements may reflect disorders such as ischemia and incipient infarction. KES utilizes the large rise in the photoelectric absorption cross section at the K-edge of elements. The introduction of a contrast agent and imaging with two energies on either side of the k-edge can give high contrast images of the vasculature in the brain.

The synchrotron geometry is ideal for doing CT of the brain, since beams are not as collimated in the vertical direction and are fan shaped in the horizontal plane. In addition, the highly collimated beams allow the detector to be placed far behind the patient, thus reducing the problem of subject to detector scatter.

The MECT system being developed at the NSLS employs monochromatic and tunable 33-100 keV x-rays from the superconducting wiggler beamline [3]. The CT configuration is that of a fixed, horizontal fan beam and a subject seated in a rotating chair. Fig. 4 shows a view of the experimental geometry looking down from above the patient. The KES studies will image the brain, large blood vessels of the head and neck, and arteriovenous malformations. DPA will obtain images that map the low Z and intermediate Z elements. The system is expected to provide 0.5 mm spatial resolution with unprecedented image contrast and accuracy of elemental quantification. At present, the research has advanced to the imaging of phantoms with animal studies planned within one year. The ultimate imaging studies of humans will take place in the SMERF facility, the synchrotron medical research facility now in operation on the X17 beamline for the coronary angiography project [25].

3.6 Transvenous coronary angiography

Certainly the most advanced of the applied medical research programs at synchrotron facilities are those doing human coronary angiography. In some ways, synchrotron medical research is synonymous with coronary angiography. The visibility of the programs to the general public, the importance of the research on coronary arterial disease, and the increasingly successful results all contribute to the aura surrounding the work. The research is known by names such as transvenous coronary angiography and synchrotron digital subtraction angiography. By any name, the field traces its origins back to the proposal that the intensity of the synchrotron x-ray beams would be high enough to allow imaging of the coronary arteries following venous injection of an iodine containing contrast agent [26].

The reason such a procedure is desirable is simply that the present arterial catheterization method (contrast agent injected directly into the coronary arteries) is too dangerous for general clinical screening and research. Certainly the images obtained are excellent and always will be necessary for acute trauma. However, for coronary artery disease research to use humans

subjects for imaging, the venous technique is highly desireable. Using conventional sources, this method proved to be a complete failure due to motion artifacts in the images and not enough flux to allow sufficient contrast between the small arteries containing highly diluted contrast agent overlying the ventricles. Even applying digital subtraction imaging at the iodine K-absorption edge proved a failure with conventional sources.

Since the first proposal, several groups around the world have taken various approaches to using the synchrotron for doing digital subtraction coronary angiography with venous injection of the contrast agent. Both differences in the x-ray optics and the types of detectors appear among the experimental groups. Pioneering work in angiography has been carried out in the Soviet Union at the Institute of Nuclear Physics [27, 28]. The programs in Japan at the Photon Factory [29, 30, 31] are working toward taking very rapid, two-dimensional exposures. They have developed two distinct optical configurations and have been testing the ideas with animal studies. In Germany at HASYLAB [32] the researchers have developed a technology much like that first described by the Stanford group in which the image is built up out of a large number of line images. In this geometry the patient must be translated through the beam. This type of image gives very good results, but takes about one second for a full scan. Although motional artifacts are virtually non-existent, the long time per scan means that phasing the images to the electro cardiogram is difficult. It is not possible to take cine angiography films. The German group has made excellent progress and has recently published their first human images [33].

The most advanced of the human coronary angiography projects is that in the United States. It was first developed at Stanford University and the early human studies were done at the Stanford Synchrotron Radiation Laboratory [34, 35]. In 1989 the project moved to the NSLS where the hardware was installed in the SMERF medical research facility [25]. SMERF is an ambulatory health care facility, fully equipped for the catheterization procedure and coronary imaging. A schematic diagram of the beamline and patient chair is shown in fig. 5. The patient moves vertically through the cross-over point of two beams, cne above the iodine K-edge and the other below the edge. Each line of data is taken in 4 milliseconds with a complete scan taken with 256 lines. Spatial resolution is presently 0.5 mm. Since October 1989, human studies have been performed at SMERF [36]. Thus far, excellent images of the right coronary artery and preliminary images of the left anterior descending coronary artery have

been obtained at the NSLS.

As an example of the present state of the coronary angiography project at the NSLS, fig. 6 compares conventional angiograms of the right coronary artery (RCA) of a female patient with a corresponding image taken at the synchrotron. The conventional images were taken before (left) and after (center) balloon angioplasty was performed. The synchrotron image (right) was obtained at the NSLS fourteen months later following venous injection of contrast agent. The patient's RCA is seen to be open in the synchrotron image. Quantification of the images shows that the spatial resolution is approaching 0.5 mm. Research programs are expected to begin soon on the treatment of post-angioplasty patients and possible plaque reduction drugs.

4.   Conclusion

It is fair to say that the medical community is just beginning to discover the world of synchroton radiation. Most of the projects discussed are in their infancies and no one can predict in what direction they will develop. Both the basic research and applied medical programs are sure to be advanced at the new facilities coming on line later in this decade. At the Advanced Photon Source at Argonne National Laboratory a Medical Imaging Center has been proposed for angiography [37]. Other major synchrotron facilities are being constructed: in the US at the Lawrence Berkeley Laboratory (Advanced Light source), in France (European Synchrotron Radiation Facility) and in Japan (Spring-8). Certainly some, if not all, of the research topics covered here will find homes in these next generation facilities. The future will certainly be exciting!

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Table 1

IMAGING AND THERAPEUTIC MEDICAL TECHNOLOGIES

Radiography	X-Rays	Angiography, Dental and Surgical X-Rays, Tumor Imaging - Projection Images
CAT Scans	X-Rays	Anatomical CT Images
Nuclear Medicine	Radioisotopes	CT Images (PETT, SPECT), Whole Body Counters, Radioisotope Therapy, Coronary Function
Radiotherapy	Ionizing Radiation and Particle Beams	Cancer Radiotherapy, Radiosurgery
Magnetic Resonance Imaging (MRI)	Radio Frequency Magnetic Fields	Anatomical CT Images
Ultrasound	Ultrasonic Acoustic Waves	Anatomical Images, Fetal Exams. Cardiac Function

Table 2

APPLICATION OF SYNCHROTRON SOURCES TO MEDICINE

Synchrotron Characteristic	Advantages
High Flux	Monochromatic Beams
Continuous Spectrum	Narrow Energy Band Tunable Source
Monochromatic Beams	No Beam Hardening
Tunable Energy Spectrum	Dose Effectiveness, Elemental Analysis, K-Edge Image Enhancement, Image/Therapy Optimization
Synchrotron Characteristic	**Disadvantages**
Planar Beam	2 Dimensional Image Constraints
Large Facilities	Limited Access, High Facility Cost

Table 3

SYNCHROTRON BASED MEDICAL RESEARCH

	TYPE OF IMAGE OR THERAPY	PRIMARY ANATOMY	RESEARCH STATUS
Angiography	Projection Image	Coronary Arteries	Human Studies
Computed Tomography	CT Image	Head and Neck	In-Vitro
Radiotherapy	External Beam	Brain Tumors	Animal Models
Mammography	Projection Image	Breast Tumors	In-Vitro
Photon Activation Therapy	Internal/External Beam Therapy	Brain	In-Vitro
X-Ray Microscopy	CT or Projection Image	Cells and Tissues	In-Vitro
Structural Biology	Crystallography	Protein Structure	In-Vitro
EXAFS	Absorption Spectroscopy	Local Molecular Structure	In-Vitro

Fig. 1   The x-ray flux from the NSLS superconducting wiggler compared w.. .. . .;ux from a conventional tungsten rotating anode x-ray tube.

Fig. 2   Survival curve of V-79 Chinese hamster cells irradiated at the NSLS a; ...;..;;c;; above (33.4 keV) and below (32.9 keV) the iodine K-absorption edge. Control cells were incubated in iodine-free medium. Iodinated cells had 16.3% IdUrd incorporated in the cellular DNA.

Fig. 3   Soft x-ray microscope image of a naturally occurring chromosomal aberration. The chromosome was obtained from the V. faba root tips. The image was recorded at the X1 beamline at the NSLS. The zone plate used to record the image was a nickel phase plate providing a Rayleigh resolution of 50 nm. Photo courtesy of S. Williams.

Fig. 4   Schematic top view of the MECT system showing the fan shaped beam, 200 mm wide, at the patient position. The patient rotates about a vertical axis in the fixed beam.

Fig. 5   Schematic diagram of the imaging hardware installed in SMERF. The patient is translated vertically through the intersection of the two beams. The energies of the beams bracket the K-absorption edge of iodine.

Fig. 6   Comparison of conventional angiograms taken before (left) and after balloon angioplasty (center) with a transvenous synchrotron coronary angiogram (right) taken at the NSLS fourteen months later (June 1991). The arrow indicates the position of the original blockage of the right coronary artery (RCA). The synchrotron image was taken in the left anterior oblique view (LAO 30°) following venous injection of contrast agent and shows that the RCA is open. The right coronary artery (RCA), aorta (AO), venous catheter (CATH) and right ventricle (RV) are identified.
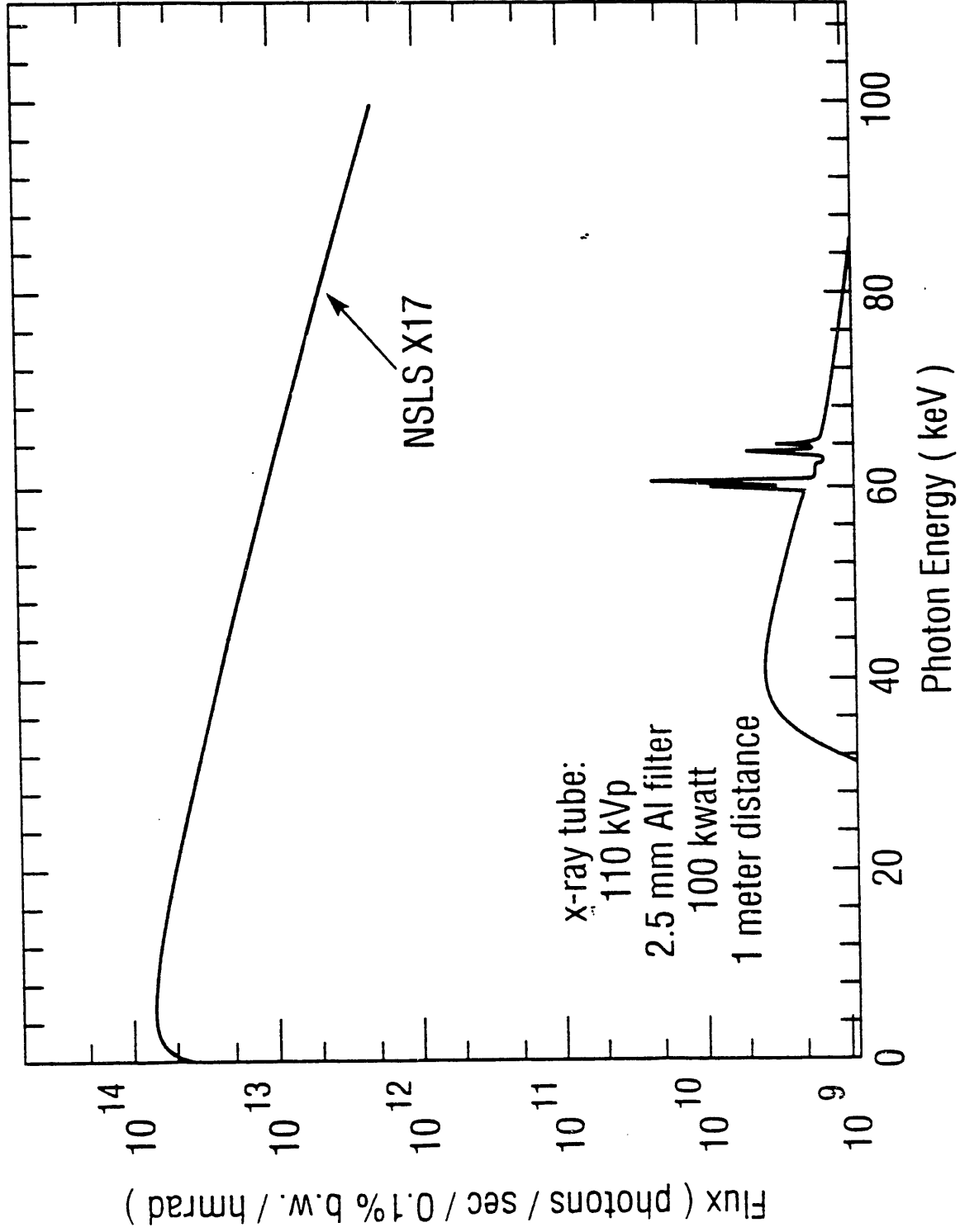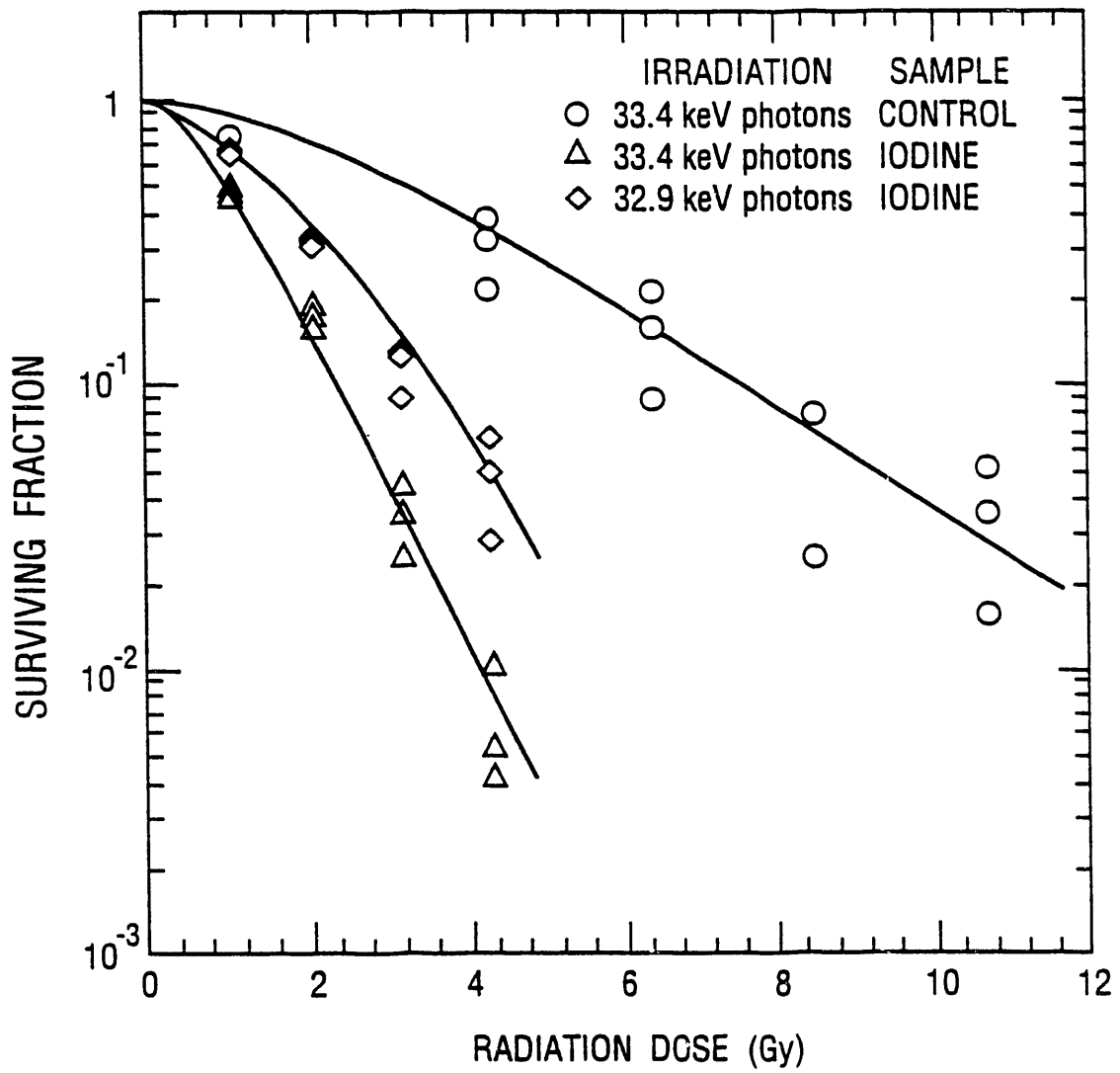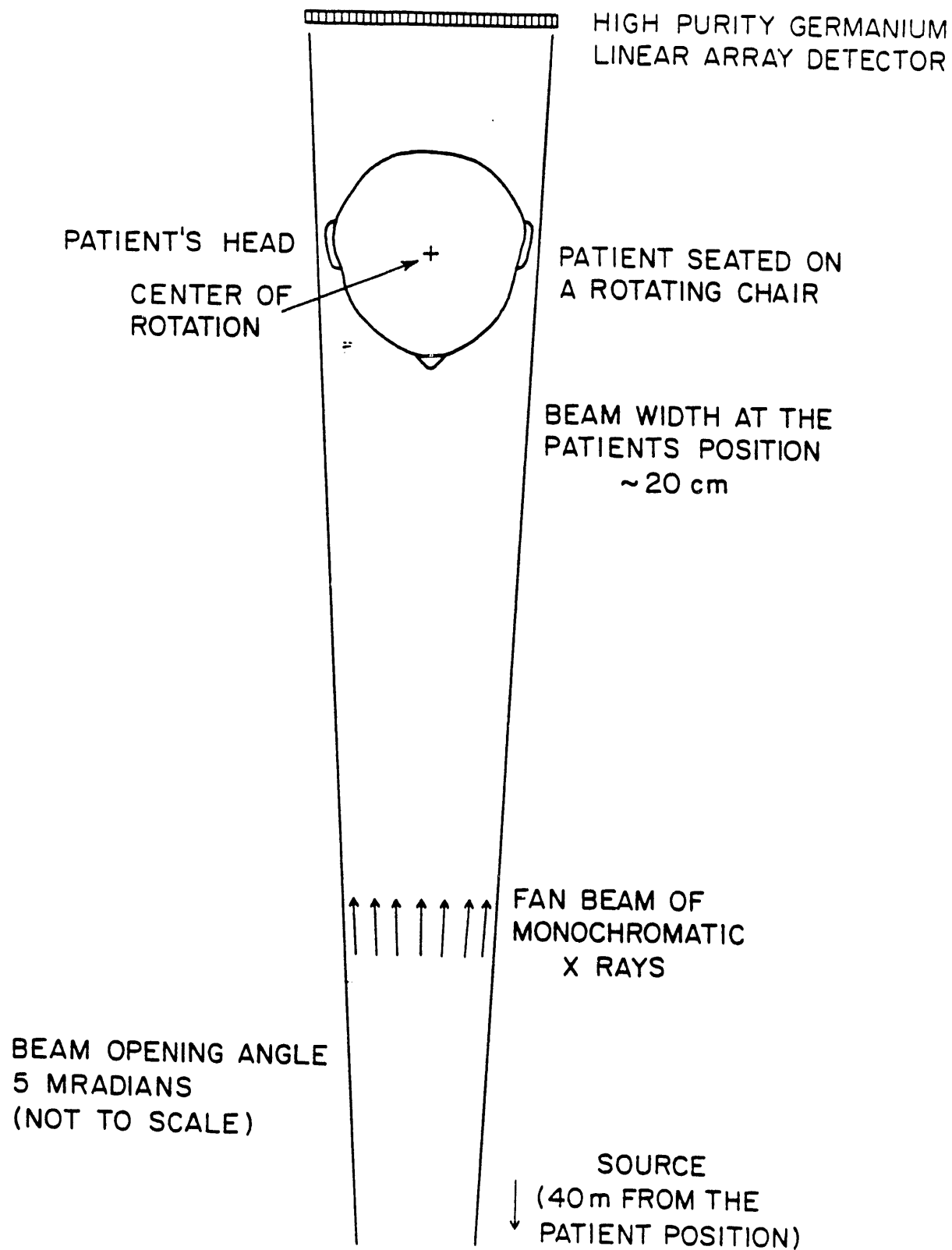
Flux Curves

Fig. 1

IRRADIATION   SAMPLE
O 33.4 keV photons CONTROL
△ 33.4 keV photons IODINE
◇ 32.9 keV photons IODINE

SURVIVING FRACTION

10^{-1}

10^{-2}

10^{-3}

RADIATION DOSE (Gy)

Fig. 2

HIGH PURITY GERMANIUM
LINEAR ARRAY DETECTOR

PATIENT'S HEAD

CENTER OF
ROTATION

PATIENT SEATED ON
A ROTATING CHAIR

BEAM WIDTH AT THE
PATIENTS POSITION
~ 20 cm

FAN BEAM OF
MONOCHROMATIC
X RAYS

BEAM OPENING ANGLE
5 MRADIANS
(NOT TO SCALE)

SOURCE
(40 m FROM THE
PATIENT POSITION)

Fig. 4

NSLS ANGIOGRAPHY BEAMLINE

IMAGE
DISPLAY

DUAL BEAM
DETECTOR

VERTICALLY
MOVING
CHAIR

PATIENT
SAFETY

DUAL ENERGY
MONOCHROMATOR

Fig. 5

END

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