Preliminary Clinical Application Study of Parametric X-rays in Diagnostic Imaging

Takashi Kaneda,¹ Kotaro Sekiya,¹ Masaaki Suemitsu,¹ Toshiro Sakae,² Yasushi Hayakawa,³ Yusuke Kawashima,⁴ Naohisa Hirahara,⁴ Hirotaka Muraoka,⁴ Kotaro Ito,⁴ Teruaki Muramatsu,⁴ Marie Ishida,⁴ and Hiroyuki Okada²

¹Departments of Radiology, ²Histology, Nihon University School of Dentistry at Matsudo, Matsudo, Chiba 271-8587, Japan

³Laboratory for Electron Beam Research and Application (LEBRA), Institute of Quantum Science, Funabashi Campus of College of Science and Technology, Nihon University, Funabashi, Chiba 274-8501, Japan

⁴Nihon University Graduate School of Dentistry at Matsudo, Oral Radiology, Matsudo, Chiba 271-8587, Japan

Article History

Received 19 March 2015

Accepted 30 March 2015

Abstract

Parametric radiation-based X-ray (PXR), one of the pioneering modalities using an accelerator, is being studied as a new kind of X-ray source in the Laboratory for Electron Beam Research and Application Institute of Quantum Science (LEBRA). The purpose of this study was to evaluate the potential of LEBRA-PXR as a new X-ray source for diagnostic imaging.

Dog mandibular tissue with malignant melanoma was examined. Simple X-ray images were taken with LEBRA-PXR at several wavelengths (12 keV, 15 keV, 18 keV, 21 keV, 24 keV, 27 keV, 30 keV). An energy subtracted image was generated with the image with the longest wavelength PXR and the image with the shortest wavelength PXR. As a control, an image was taken with conventional X-ray (40 kV, 125 mA, 40 msec; effective energy 21 keV). Simple X-ray images were taken with LEBRA-PXR, and the energy subtracted and conventional X-ray images were compared with the histopathological stained images. Compared to conventional X-ray images, LEBRA-PXR images showed contrast related to different wavelengths, reflecting histological differences between tissues. Compared with the histological findings, malignant tumor images with LEBRA-PXR were clearer than conventional X-ray images.

Using LEBRA-PXR, a type of nearly perfectly monochromatic X-ray source imaging, the images of the malignant tumor displayed different contrasts from conventional X-ray images. LEBRA-PXR is a useful diagnostic imaging tool using a new X-ray source.

Keywords :

Parametric X-ray,
New X-ray source,
Clinical application

Introduction

Since Wilhelm Conrad Rontgen discovered X-rays in 1895, the application of X-rays has been expanding and is one of the most important applications in medical imaging and radiation therapy. Currently, while X-rays are applied to the more delicate medical and life sciences, more brilliant, powerful, and coherent X-ray sources are needed for not only the basic sciences, but also for applications to the biological sciences.

Pioneering studies for these are being performed among

the giant electron accelerator laboratories throughout the world, such as the European XFEL at Hamburg, the LCLS at Stanford, the KEK-PF at Tsukuba, and the Spring 8 at Harima (1-10). Parametric radiation-based X-ray (PXR), one of the pioneering modalities using an accelerator, is being studied as a potential new X-ray source in the Laboratory for Electron Beam Research and Application Institute of Quantum Science (LEBRA) (11).

PXR is generated using a relatively small linear accelerator (LINAC; 125 MeV) and a silicon crystal, with unique features that differ from conventional X-ray. PXR is a kind of electromagnetic radiation phenomenon that is produced by interaction between a relativistic charged particle and a

Correspondence to :

Takashi Kaneda

E-mail : kaneda.takashi@nihon-u.ac.jp

Fig. 1 Principle and generation of parametric X-rays

Parametric X-ray radiation is generated by the motion of electrons inside a crystal; the emitted photons are diffracted by the crystal, and the radiation intensity is critically dependent on the parameters of the crystal structure. The generated PXR radiation angle and the incident electron beam angle are the same, consistent with Bragg's law. Because the wavelength, or X-ray energy, of the generated PXR is defined by the incident angle of the electrons, the PXR wavelength is arbitrarily determined by selecting the incident electron beam angle. The tunability of the X-ray wavelength has previously been possible only at giant accelerator laboratories.

(d : crystal lattice spacing, θ : incident and reflection angle, n : constant number, ϕ : incident angle of charged particles.)

periodic structure found in a crystalline material(12).

PXR has several unique characteristics, such as wavelength tunability, a nearly perfectly parallel beam, a nearly perfect monochromatic beam, and high coherency(13, 14) However, only a few experiments have been reported on the practical applications of PXR.

The purpose of this study was to evaluate the potential of LEBRA-PXR as a new X-ray source for diagnostic imaging.

Materials and Methods

Dog mandibular tissue with malignant melanoma was examined. Simple X-ray images were taken with LEBRA-PXR at several wavelengths (12 keV, 15 keV, 18 keV, 21 keV, 24 keV, 27 keV, 30 keV). An energy-subtracted image was generated with the image with the longest wavelength PXR and the image with the shortest wavelength PXR. As a control, an image was taken with conventional X-ray (40 kV, 125 mA, 40 msec; effective energy 21 keV).

The subject tissue was cut, H&E stained, and viewed with a microscope after X-ray examinations. Simple X-ray images were taken with LEBRA-PXR, and the energy subtracted and conventional X-ray images were compared with the histopathological findings.

Parametric X-ray

PXR radiation is generated by the motion of electrons inside a crystal, whereby the emitted photons are diffracted

by the crystal, and the radiation intensity is critically dependent on the parameters of the crystal structure 23 (Fig.1). The relationship between the generated PXR radiation angle and the incident electron beam angle is the same, similar to the condition of Bragg's law. Because the wavelength, or X-ray energy, of the generated PXR is defined by the incident angle of the electrons, the PXR wavelength can be determined arbitrarily by selecting the incident electron beam angles. The tunability of X-ray wavelength has previously only been possible at giant accelerator laboratories.

Results

Compared to conventional X-ray images, LEBRA-PXR images showed contrast related to different wavelengths, reflecting histological differences between tissues (Fig.2). Energy subtraction imaging with LEBRA-PXR offered more soft tissue and osteolytic bony image information related to morphology and structure(Fig. 3). Comparing the histological findings, malignant tumor images with LEBRA-PXR were clearer than conventional X-ray images.

Discussion

In our preliminary experimental study, compared to conventional X-ray images, LEBRA-PXR images showed contrast related to different wavelengths, reflecting histological differences between tissues, such as malignant

Fig. 2 LEBRA-PXR

Fig. 3 Principle and generation of parametric X-rays

Parametric X-ray radiation is generated by the motion of electrons inside a crystal; the emitted photons are diffracted by the crystal, and the radiation intensity is critically dependent on the parameters of the crystal structure. The generated PXR radiation angle and the incident electron beam angle are the same, consistent with Bragg's law. Because the wavelength, or X-ray energy, of the generated PXR is defined by the incident angle of the electrons, the PXR wavelength is arbitrarily determined by selecting the incident electron beam angle. The tunability of the X-ray wavelength has previously been possible only at giant accelerator laboratories.

(d : crystal lattice spacing, θ : incident and reflection angle, n : constant number, ϕ : incident angle of charged particles.)

lesions of soft tissue and osteolytic bony image information related to morphology and structure.

LEBRA-PXR is generated by the interaction of a silicon crystal and electrons accelerated by the LINAC, and then the radiation has a pulse structure, a macro pulse structure and a micro pulse structure, due to the LINAC system. This short net exposure time of PXR generated by a LINAC is an excellent advantage for future medical application to decrease radiation effects on the human body.

The LEBRA-PXR generator has a unique double-crystal system that allows the PXR radiation direction to always fit in the same direction, which facilitates the experimental setting of LEBRA-PXR studies(14-17). The total length of

the LEBRA-PXR generator is only 2 m in comparison with the length needed at the giant accelerator laboratories, being several hundred meters to several kilometers in size. A smaller size is needed for PXR applications in diagnostic medical imaging and treatment in hospital.

As X-ray absorption of material relates to the absorption coefficients of the component elements, and the coefficients are related to the X-ray wavelength, then changing the X-ray wavelength causes variation in the contrast of the image, especially when the object is composed of different elements. The merit of monochromatic X-rays for biological and medical studies was pointed out as early as 1947(18). The wide X-ray wavelength tunability of LEBRA-PXR can

Fig. 4 Conventional X-ray, LEBRA-PXR images, and histological findings of a dog melanoma specimen

Energy subtraction imaging with LEBRA-PXR offers more soft tissue and osteolytic bony image information related to morphology and structure. Comparing histological findings, the malignant tumor images with LEBRA-PXR are clearer than those of the conventional X-ray images.

be put into practice by tilting the target silicon crystal, ranging from 0.248 nm (5.00 keV) to 0.0344 nm (36.0 keV). The emitted radiation is an almost perfect monochromatic X-ray. Calculation of the estimated bone absorption for the monochromatic X-ray was carried out, and the calculated values were compared with those read from the images of the plastic-standard equivalent to bone. Images with different X-ray wavelengths were also taken for malignant tumors, as in the present study.

Use of monochromatic X-rays has potential for application in biological and medical fields(18-22). For quantitative bone analysis, monochromatic X-rays would be useful not only for local bone mineral content(BMC) and bone mineral

density(BMD) measurements, but also for determination of bone body mineral content(TBBMC) (23, 24). LEBRA-PXR has been increasingly found to be superior because of its ease of use and simple settings(14).

Compared to the other facilities, the advantages of LEBRA-PXR as a source of X-ray are: produced by a small LINAC, small and short X-ray generator, easy wavelength tunability, fixed X-ray radiation direction, highly monochromatized, slight divergence of wavelength in the horizontal direction, and a wide imaging or detecting area. At present, the detector system is not yet suitable for more sensitive and precise investigations, but it is enough to evaluate the characteristics of PXR. It is hoped that a

compact, coherent, wavelength-tunable, and brilliant X-ray source can be produced for biological and medical applications, as well as for basic and applied sciences. The results of the present study show that the required X-ray source can be built in the same manner as the LEBRA-PXR system.

Conclusion

Using the images of LEBRA-PXR, which uses a nearly perfect monochromatic X-ray source, displays malignant tumors as differently contrasted from those of conventional X-ray images; as such, LEBRA-PXR is a useful new diagnostic imaging tool using a new X-ray source.

Acknowledgments

This work was supported in part by JSPS KAKENHI Grant-in-Aid for Scientific Research (C) Grant Number 24592844 and by the Nihon University Multidisciplinary Research Grant for 2012–2013 (Sogo: 12–19, 13–19).

References

- Spiller RF, Gudat W, Panessa BJ, Zadunaisky ZA, Sedat J: High-resolution soft X-ray microscopy. *Science* 197: 259–260, 1977.
- Kirz J, Sayre D: Soft X-ray microscopy. *Nucl Instrum Methods Phys Res A* 246: 695–697, 1986.
- Suckewer S, Skinner CH: Soft X-ray lasers and their applications. *Science* 247: 1553–1557, 1990.
- Kirz J, Jacobsen C, Howells M: Soft X-ray microscopes and their biological applications. *Quarterly Rev Biophys* 28: 33–130, 1995.
- Jacobsen C: Soft X-ray microscopy. *Trends Cell Biol* 9: 44–47, 1999.
- Abraham-Peskir JV: X-ray microscopy with synchrotron radiation: Applications to cellular biology. *Cell Mol Biol* 46: 1045–1052, 2000.
- Chao W, Harteneck BD, Liddle JA, Anderson EH, Attwood DT: Soft X-ray microscopy at a spatial resolution better than 15 nm. *Nature* 435: 1210–1213, 2005.
- Stefano B, Biryukov VM: The future looks bright for particle channeling. *CERN Courier*, 2006.
- Ogura T: Direct observation of unstained wet biological samples by scanning-electron generation X-ray microscopy. *Biochem Biophys Res Commun* 391: 198–202, 2009.
- Young L, Kanter EP, Krässig B, Li Y, March AM, Pratt ST, Santra R, Southworth SH, Rohringer N, DiMauro LF, Doumy G, Roedig CA, Berrah N, Fang L, Hoener M, Bucksbaum PH, Cryan JP, Ghimire S, Glownia JM, Reis DA, Bozek JD, Bostedt C, Messerschmidt M: Femtosecond electronic response of atoms to ultra-intense X-rays. *Nature* 466: 56, 2010.
- Hayakawa, Y: Parametric X-ray radiation and possibility of monochromatic X-ray source using a linac. KURRI-KR-43, Advanced Research of Quantum Beam Science (III) 43–49, 2000.
- Baryshevsky VG, Feranchuk ID, Ulyanenko AP: Parametric X-Ray Radiation in Crystals. Springer, Tracts in Modern Physics, 213: 171, 2005.
- Sones B, Yaron D, Robert B: Production and application of a novel energy-tunable X-ray source at the RPI LINAC. *Nucl Instrum Methods Phys Res B* 261: 98–101, 2007.
- Wilkins SW, Gureyev TE, Gao D, Pogany A, Stevenson AW: Phase-contrast imaging using polychromatic hard X-rays. *Nature* 384: 335–338, 1996.
- Momose A, Takeda T, Itai Y, Hirano K: Phase-contrast X-ray computed tomography for observing biological soft tissues. *Nature Medicine* 2: 473–475, 1996.
- Shapiro D, Thibault P, Beetz T, Elser V, Howells M, Jacobsen C, Kirz J, Lima E, Miao H, Neiman AM, Sayre D: Biological imaging by soft X-ray diffraction microscopy. *Proc Natl Acad Sci* 102: 15343–15346, 2005.
- Hayakawa Y, Sato I, Hayakawa K, Tanaka T: Simulations to the project of a PXR based X-ray source composed of an electron linac and a double-crystal system. *Nucl Instrum Methods Phys Res B* 27: 32–40, 2004.
- Clark GL: Medical, biological and industrial applications of monochromatic radiography and microradiography. *Radiology* 49: 483–495, 1947.
- Momose A, Fukuda J: Phase-contrast radiographs of non-stained rat cerebellar specimen. *Med Phys* 22: 375–380, 1995.
- Momose A: Demonstration of phase-contrast X-ray computed tomography using an X-ray interferometer. *Nucl Instrum Methods Phys Res A* 352: 622–628, 1995.
- Takeda T, Momose A, Hirano K, Haraoka S, Watanabe T, Itai Y: Human carcinoma: early experience with phase-contrast X-ray CT with synchrotron radiation – comparative specimen study with optical microscopy. *Radiology* 214: 298–301, 2000.
- Nakada H, Sakae T, Suwa T, LeGeros RZ, Gunji A, Kato T, Kozawa Y, Kobayashi K: Observation of Newly Formed Bone Around Implants Using Parametric X-ray. *J Hard Tissue Biology* 14: 1–4, 2005.
- Nakada H, Sakae T, Suwa T, Machida T, LeGeros RZ, Gunji A, Kato T, Kobayashi K: Comparison between parametric X-ray and dental X-ray for observing new bone formation in implant surroundings. *Nihon Univ J Oral Sci* 31: 110–115, 2005.
- Nakada H, Sakae T, Suwa T, LeGeros RZ, Gunji A, Kato T, Kobayashi K: Observation of Newly Formed Bone Around Dental Implant Using Parametric X-ray. *Key Engineering Materials*, 309–311: 31–34, 2006.