

# STUDY OF MEDICAL APPLICATIONS OF COMPACT LASER-COMPTON X-RAY SOURCE\*

Y. Hwang<sup>†</sup>, T. Tajima, University of California, Irvine, CA USA 92697  
G. G. Anderson, D. J. Gibson, R. A. Marsh, C. P. J. Barty,  
Lawrence Livermore National Laboratory, Livermore, CA USA 94550

## Abstract

Compton scattering of laser photons by a relativistic electron beam produces monoenergetic, tunable and small source size X-rays similar to synchrotron light sources in a very compact setting, due to the shorter undulator period of lasers. These X-ray sources can bring to every hospitals advanced radiology and radiotherapy that are currently only being conducted at synchrotron facilities. Few examples include phase contrast imaging utilizing the micron-scale source size, K-edge subtraction imaging from two monoenergetic X-rays at different energies and radiation therapy using radiosensitization of high-Z nanoparticles. At LLNL, 30 keV X-rays have been generated from the 30 MeV X-band linac, and the X-rays have been characterized and agree with the modeling very well. This source is being used to study the feasibility of aforementioned medical applications. Experimental setup of K-edge subtraction of contrast agents are presented, demonstrating the low-dose, high-contrast imaging potential of the light source. Plans to study enhanced radiotherapy using Gold nanoparticles with the upgrade of the machine to higher energies are discussed.

## INTRODUCTION

Medical imaging and therapy has seen great advancements since the advent of synchrotron radiation (SR), utilizing its bright, monochromatic and tunable X-ray beam of very small source size [1]. However, medically relevant X-ray energies (keV to MeV) can only be obtained with GeV-class accelerators, mostly through undulator radiation. Such facilities are too large and costly, limiting the accessibility of SR radiology and radiotherapy. Therefore, a compact X-ray source that produces SR-like beam will provide a huge boost and aid in popularization of medical applications of SR.

X-ray and  $\gamma$ -ray generation by laser-Compton scattering (LCS) is being studied worldwide for its potential as a compact synchrotron-quality X-ray source [2–6]. LCS can be seen as SR with the undulator replaced by the laser's electric field, therefore shortening the scattered photon frequency by more than 3 orders of magnitude. In a head-on collision of a laser and an electron beam, photons backscattered in the electron beam direction gain energy up to a factor of  $4\gamma^2$ , where  $\gamma$  is the electron beam Lorentz factor. Using

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<sup>†</sup> yoonwooh@uci.edu

optical lasers, hard X-rays in the range of 10-100 keV can be produced with electron linear accelerators with energies less than 50 MeV. Such accelerators are commonly used in hospitals for external beam therapy. Hence, LCS can provide a breakthrough in medical imaging and therapy by introducing SR to every hospital. In the following, notable medical SR applications are discussed and its feasibility study plan using the LLNL Compact Laser-Compton X-ray Source is presented.

## MEDICAL IMAGING WITH LCS

Conventional radiology relies on Bremsstrahlung X-rays produced by an electron beam of tens of keV hitting an anode target. It is very compact and simple to operate, but due to its broad spectrum the patient receives unnecessary dose from low-energy X-rays which also reduces the quality of the image especially in the case of computed tomography (CT) due to beam hardening. One may use a filter material to block the low-energy portion or use a target possessing a specific fluorescent radiation peak, at the loss of overall flux. In contrast, a monochromatic beam as in the case of SR or LCS can significantly reduce the patient dose while improving the resolution of the image. Monochromatic beams can also provide a much higher contrast for contrast agent imaging if the contrast agent's K-edge is just below the beam energy.

### *K-edge Subtraction Imaging*

The energy tunability of LCS, in the form of either direct change in electron beam energy, different colored laser, change in interaction angle or change in observation angle, enables a new imaging technique known as K-edge subtraction (KES). In this scheme, an image with X-ray energy just above the K-edge of the contrast agent is subtracted from a similar image but with the X-ray energy just below the K-edge. Since the attenuation coefficient of body parts not containing the contrast agent are nearly constant between the two energies as shown in Fig. 1, these features are completely subtracted and only the contrast agent image remains.

### *Phase Contrast Imaging*

For hard X-rays in body-like matter, the real part of the refractive index is larger than the imaginary part, causing bigger changes in phase than in absorption. The phase change in matter can be detected in a number of ways. With a spatially coherent beam one can observe directly the refractive edge-enhancement effect [7]. With a monochromatic beam, X-ray diffraction can be used to detect the small angle refractions of the beam [8]. Further, various interferometric

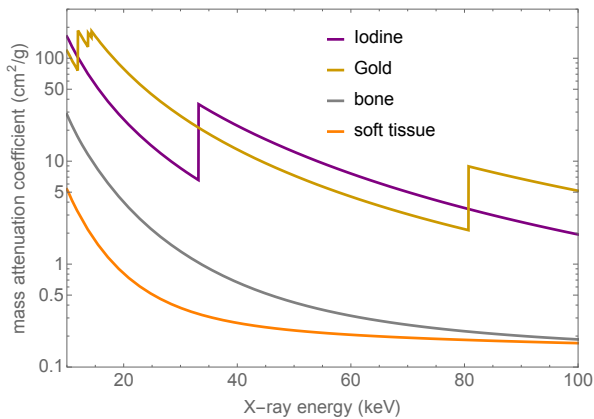


Figure 1: Mass attenuation coefficients for body tissues and contrast agents.

methods have been used to extract detailed phase shift information [9, 10]. These techniques have been successfully demonstrated using LCS by Bech et al. [11].

### RADIOTHERAPY WITH LCS

Current X-ray radiotherapy is mostly carried out using MeV beams created from medical linacs or characteristic  $\gamma$ -rays from radioisotopes, but there is a new technique using <100 keV beam to trigger Auger cascade of high-Z nanoparticles placed near cancer cells [12]. Nanoparticles accumulate in tumors due to the enhanced permeability and retention (EPR) effect, where abnormal blood vessel structures in tumors allow macromolecules to permeate more readily and be retained longer than in normal tissues. Selectivity can be further increased by attaching tumor targeting molecules to the surface of the nanoparticles. Furthermore, the nanoparticles can serve as contrast agents as well as a radiosensitizer as in image-guided radiotherapy (IGRT) [13], enabling diagnostics and therapy to be performed with the same beam and drug, also known as theranostics. Combined with the monochromaticity of LCS, the dose selectivity can be greatly increased.

### LLNL COMPACT LASER-COMPTON X-RAY SOURCE

The laser-Compton X-ray source at LLNL is an X-band 30 MeV linear accelerator LCS light source, producing 30 keV X-rays by a head-on collision of the electron beam with a 532 nm laser beam [14, 15]. Source parameters are given in Table 1.

The accelerator currently has a 7 MeV photogun and one accelerating section; in the future, installation of a second accelerating section and a pulse compressor can bring the energy up to >85 MeV, generating >250 keV Compton X-rays. The X-rays have been characterized and agrees well with simulations [16, 17]. A sample image of the X-ray beam is shown in Fig. 2.

Table 1: LLNL LCS Source Parameters

| e <sup>-</sup> beam parameters |               | photon parameters |                    |
|--------------------------------|---------------|-------------------|--------------------|
| bunch charge                   | 50-200 pC     | laser energy      | 750 mJ             |
| bunch length                   | 2 ps          | pulse length      | 6.5 ns             |
| spot size                      | 10-30 $\mu$ m | beam waist        | 50 $\mu$ m         |
| No. bunches                    | 1-16          | wavelength        | 532 nm             |
| emittance                      | 0.3 $\mu$ m   | X-ray energy      | 30 keV             |
| RF                             | 11.424 GHz    | X-ray flux        | $3 \times 10^6$ /s |
| energy                         | 30 MeV        | on-axis b/w       | 0.6 %              |
| energy spread                  | 0.03 %        | rep. rate         | 10 Hz              |

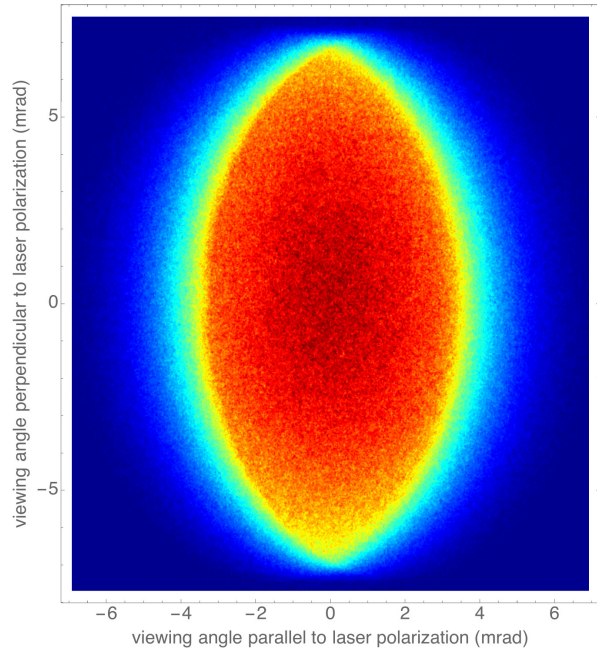


Figure 2: Laser-Compton X-ray image through a fused silica back-thinned optic.

### K-EDGE SUBTRACTION EXPERIMENT

As a demonstration of K-edge subtraction imaging in angiography/nanoparticle radiology, we are designing an experiment using various concentrations of Ag solution in capillary tubes. Silver is chosen because its K-edge (25.5 keV) lies within our machine's X-ray range and its solution, either in ionic form or as nanoparticles, is readily available. Iodine is a widely used contrast agent in medical imaging and thus would be preferred as a more realistic test, but its K-edge (33.2 keV) is too close to the maximum energy of the machine (34 keV), which means there is only a small region where it will be above the Iodine K-edge. In addition, our imaging systems incorporate Iodine in scintillators (CsI(Tl)) or imaging plates (BaFBr<sub>0.85</sub>I<sub>0.15</sub>), leading to concerns about abrupt light yield change at the K-edge, which would invalidate the assumption that intensity does not change considerably between above-K-edge and below-K-edge images where the contrast agent is not present [18]. When the accelerator's energy upgrade is complete, we can try contrast agents with

higher K-edge, such as Gd (50.3 keV) and Au (80.7 keV). Capillary tubes made of PTFE or PI (Kapton) are being considered for ones with inner diameter less than 0.5 mm, while larger tubes are available in a wider variety of materials.

## AUGER THERANOSTICS

In order to study the viability of LCS in Auger theranostics, nanoparticles and biological samples including live cells are required. If active cancer-targeting agents are to be loaded to the nanoparticles, a comparison study of cancer cells and living cells can be made in a similar fashion. If one only relies on the passive EPR effect, a live animal will be required to grow the vascular structures for the tumor. Gold is the favored nanomaterial most widely studied for Auger radiosensitization, and it has been shown that the X-ray beam need not be above the Au K-edge in order to see the enhancement effect [19], so the current energy at 30 keV suffices for the therapy experiment. However, as mentioned earlier, if one is to image the nanoparticles using K-edge subtraction, energy must be increased or Ag nanoparticles would have to be used. The effectiveness of KES for Au is yet uncertain, as attenuation is quite low at such high energy (i.e. the K-edge jump is small) and simple contrast imaging at a lower energy where Au's attenuation is much higher than that of soft tissue may give better contrast than KES.

## CONCLUSION

Advantages of LCS over SR and conventional X-ray sources in medical settings have been discussed, highlighting the K-edge subtraction imaging and Auger theranostics. We are currently planning to study these techniques with the LLNL laser-Compton X-ray source, either in the current configuration or after the energy upgrade which will enable more types of contrast agents to be used.

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