Development of Novel Ultrafast-Laser-Based Micro-CT System for Small-Animal Imaging

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Abstract— **We investigated the performance of an ultrafast-laser-based x-ray source as a possible replacement of a microfocal X-ray tube in a micro-CT system for small-animal imaging. Using a number of solid targets (Ge, Mo, Ag, Sn, BaF_2, La, and Nd) with matching filters, we optimized conditions for x-ray generation and measured x-ray spectra, conversion efficiency, x-ray fluence, and x-ray focal-spot size. We obtained images of small animals. X-ray spectra created by ultrafast laser are advantageous for micro-CT imaging because most of the emission is in narrow characteristic lines. The spectra could be rapidly changed and matched to the imaging task (e.g. animal thickness and density). This novel x-ray source can be also easily applied in dual-energy micro-CT for small-animal imaging with suitable contrast agent (e.g. I-, Ba-, or Gd-based) and matching targets and filters for low- and high-energy beams. We have established that the effective x-ray focal-spot size can be smaller than 5 µm and that the average power can surpass the power delivered by a microfocal x-ray tube with 5 µm focal-spot size.**

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I. Introduction

The microfocal x-ray tube used as an x-ray source in micro-CT for small-animal imaging suffers from severe limitations such as the following: i) selection of the anode material is limited to a few metals (Cu, Mo, W); ii) the x-ray spectra produced are relatively broad; iii) the maximum power that may be applied to the tube is limited by the rate of the anode cooling (typically below 10 W) [1,2]. We investigated the possibility of substitution of the microfocal x-ray tube with a novel, ultrafast laser-based x-ray (ULX) source. This new source provides narrow x-ray emission lines that can be easily tuned to the imaging task, (e.g. maximize contrast while minimizing the radiation dose for a given animal). The narrow emission lines used for imaging, instead of broad bremsstrahlung, assure better dose utilization and limited beam-hardening effect. The average power of ULX exceeds the maximum power of a microfocal x-ray tube, thus allowing faster scans. ULX can be also be easily applied in dual energy micro-CT for small animal imaging with suitable contrast agent (e.g. based on I, Ba or Gd), and matching targets and filters for low- and high-energy beams.

II. Ultrafast Lasers

The invention of chirped-pulse amplification (CPA) in the mid 1980's [3] and the availability of high-quality Ti:Sapphire crystals allowed achievement of very high optical power density (10^{18}–10^{20} W/cm^2) delivered to the target. This is delivered by a laser beam from a compact (table-top) terawatt (1 TW = 10^{12} W) lasers with femtosecond (1 fs = 10^{-15} s) pulse duration. We note that a conventional x-ray tube has electron power density at the target below 10^9 W/cm^2. The concept of CPA is illustrated in Fig. 1. Such ultra-high intensities are possible because a very short laser pulse can be focused to a spot ~5 µm or smaller in diameter. We note that the peak electric field of such an intense beam exceeds 10^{11} V/m.

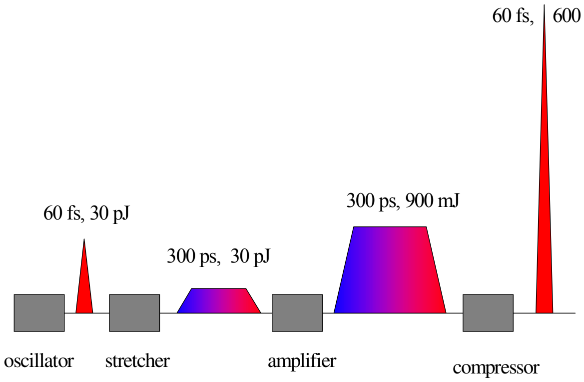

Fig. 1. Chirped-pulse amplification concept.

III. X-RAY PRODUCTION BY ULTRAFAST LASERS

When the laser light-power surface density on the solid target exceeds ~5×10^{12} W/cm^2, a very thin layer of inhomogeneous, cold and dense plasma is formed. During the interaction of the laser with the solid or preformed plasma, up to 40% of the laser energy is transferred to suprathermal (hot) electrons through resonance absorption, vacuum heating, **J**×**B** heating, and other effects [4]. Many of the hot electrons leave the dense-plasma region and consequently a very strong space-charge field is set up within the plasma. This electric field attracts a significant part of the hot electrons, some of which penetrate the plasma and the target. This results in a short lasting burst of incoherent x-rays that consist of continuous bremsstrahlung and characteristic emission lines. The continuous emission can span from several tens of keV to a few MeV depending on the parameters of the laser and the plasma, whereas the emission lines are in the range of 1–100 keV depending on the atomic number of the target material. The x-ray pulse lasts longer than the laser pulse, generally ranging from several hundreds of femtoseconds to several picoseconds. The x-ray source size is larger than the laser spot size. Examples of ULX spectra are shown in Figs. 2–4.

X-ray spot sizes were measured (using the tungsten knife-edge method, with the edge placed perpendicular and parallel to the plane of incidence) for a number of solid targets (including Ge, Mo, Ag, and Sn). Parallel to the plane of incidence, spot sizes are ~2–3 times those measured perpendicular to that direction (valid for all materials). We observe that the x-ray spots are approximately elliptical in shape 2–5 µm × 4–15 µm, depending on the laser beam focusing and the pulse duration. If a deformable mirror is used, a focal spot as small as 1.6-µm can be achieved [5].

In contrast to a microfocal x-ray tube, there is no upper limit to the power that can be delivered by an ultrafast laser to a solid target. This is because the ultrafast laser pulse ablates a small crater (5 µm diameter) on the target surface, and fresh target surface is exposed to each laser shot. Presently, a state-of-the-art ultrafast laser can deliver up to 50 W power to a focal spot smaller than 4 µm.

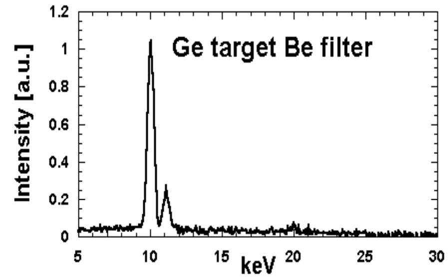

Fig.. 2. ULX spectrum created by Ge target with 1 kHz laser at Center for Ultrafast Optical Science, University of Michigan.

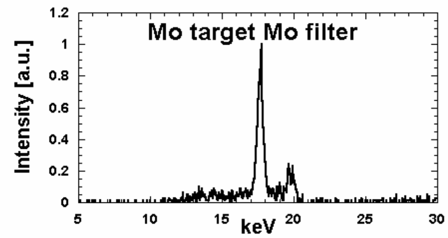

Fig. 3. ULX spectrum created by Mo target with 10 Hz laser at INRS-Énergie et Matériaux, Université du Québec.

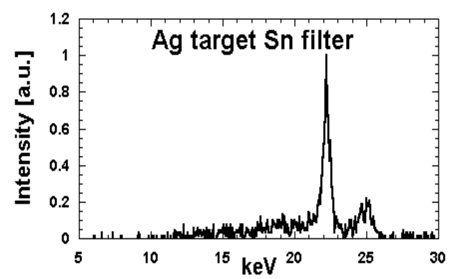

Fig. 4. ULX spectrum created by Ag target with 10 Hz laser at INRS.

IV. ENERGY OPTIMIZATION FOR MICRO-CT

ULX is well suited for energy optimization tasks in micro-CT for small animals. It has been established that, in order to achieve best contrast resolution with a minimum number of photons, for single energy imaging, the average total linear absorption coefficient $\langle\mu(E)\rangle$ of the sample has to match the characteristic dimension of the sample (D) [2,6]

$$\langle \mu(E) \rangle \approx \frac{2}{D} \qquad (1)$$

Depending on small-animal composition, the optimal energy is in the 10–30 keV range for D = 10 mm. In the case of ULX, the energy tuning can be easily accomplished by selecting a suitable ultrafast laser target; for example, a Ge target will produce lines around 10 keV, while a Sn target will produce lines around 25 keV. We note that the optimal contrast resolution at minimum dose might result in a different optimal

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energy depending on the targeted-organ dose location [7]. We expect dose savings while using ULX, because of better matching of the x-ray spectrum to the animal thickness and density. We plan to investigate this issue experimentally using thermoluminescent dosimeters (TLDs) and Monte Carlo modeling.

K-edge subtraction micro-CT is highly valuable when a contrast agent (containing I, Ba, Gd,…) is used. This technique requires an energy difference as small as possible between high- and low-energy beams that have to bracket the absorption line of contrast agent. While this is difficult with a conventional microfocal x-ray tube, it is quite practical with ULX. For example, for a contrast agent with iodine (K-edge at 33.2 keV), suitable targets include BaF_2 (emission lines at 32.2 and 31.8 keV) for the low-energy beam and Nd (emission lines at 37.4 and 36.8 keV) for the high-energy beam.

IV. Small-Animal Images Obtained with ULX References

An example of a small-animal image obtained with ULX in a single-energy mode is shown in Fig. 5.

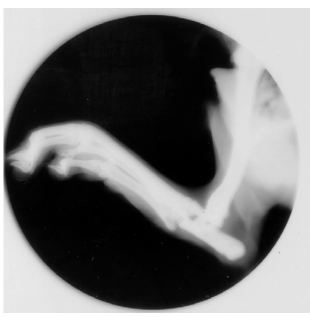

Fig.. 5 Distal hind limb of a mouse ~20 weeks old, 10 Hz laser at INRS, Mo target, Mo filter, SOD = 15.0 cm, SID = 30.0 cm, pulse duration: 60 fs, energy per pulse: 300 mJ, p-polarization, contrast: 10^{-6}, λ = 400 nm, hot electron temperature: 20 keV, repetition rate: 10Hz, Fuji EC-MA cassette/AD film used as an image detector

An example of a K-edge subtraction image small of a small animal obtained with ULX in a dual energy mode is shown in Fig. 6.

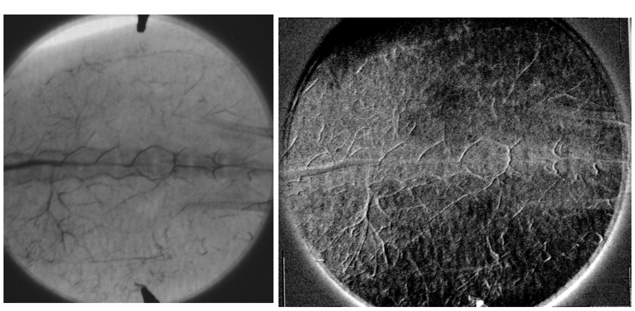

Fig.. 6. Left: image of a rat's vasculature containing Iodinated contrast agent obtained using ULX 10 Hz laser at INRS with Nd target and Nd filter. Right: differential Nd–BaF_2 image of the same rat obtained after subtraction, from the image on the left, of a ULX image obtained with BaF_2 target and I filter. Laser parameters were the same as in Fig. 5.

V. Design of Micro-CT System with Ultrafast Laser-Based X-Ray Source

A simplified block diagram of a proposed ultrafast-laser-based microtomography system is shown in Fig. 7. The system is very similar to a conventional one, but with the microfocal tube substituted by a laser target chamber. However, since a single laser-beam pulse focused on a solid target creates an ablation crater ~5–20 µm in diameter and 1–2 µm in depth (depending on pulse duration and irradiation conditions), a fresh target surface has to be exposed to each laser shot. Therefore, the target transport system has to be very accurate and has to position the fresh target surface with 1 µm accuracy for each successive laser shot. For this purpose a feedback system needs to be developed and implemented for precise beam positioning and target rastering. Adaptive optics to correct for the laser wave-front distortion and to pre-compensate for the aberrations caused by the focusing optics will be used, allowing laser-beam focusing within the diffraction limit (~1.5 µm).

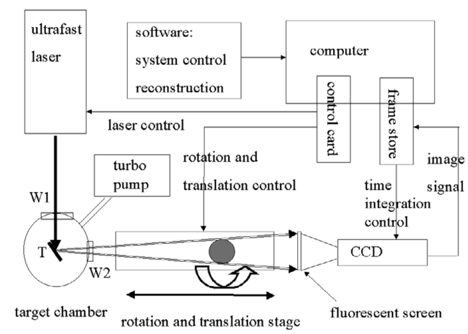

Fig. 7. Simplified block diagram of proposed ultrafast-laser-based micro-CT system for small-animal imaging.

The system specifications include:

- 30×30×30 mm^3 3D field of view
- specimen size up to 30 mm diameter and 120 mm long (in 4 bed positions)
- spatial resolution 4–50 µm
- cone-beam acquisition geometry
- CCD detector with modified the x-ray converter screen

We plan to investigate, in collaboration with Radiation Monitoring Devices, Inc., application of microcolumnar CsI(Tl) films on various substrates that will maximize spatial resolution and light output, while minimizing the associated noise for ULX. The CsI(Tl) vapor-deposition protocols to manufacture 10–180 mm thick films required for 10–50 keV x-ray detection will be modified under this development. The specific goal will be develop screens that will maximize spatial resolution and light output, while minimizing the associated noise.

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We plan to develop new imaging protocols to take full advantage of the flexible x-ray spectra provided by ULX in single and multiple energy modes.

VI. Conclusions

In summary, our initial studies on application of ULX as a replacement for a microfocal x-ray tube in a micro-CT system for small-animal imaging indicate that a novel x-ray source might yield the following advantages: shorter scan duration, lower radiation dose, and limited beam-hardening artifact; and it might allow practical implementation of dual-energy imaging for K-edge subtraction with a suitable contrast agent, containing, for example, I, Ba, or Gd.

VII. References

[1] M.J. Flynn, S.M. Hames, D.A. Reiman, and S.J. Wilderman, “Microfocused x-ray source for 3-D microtomography,” *Nuc. Instrum Methods Phys Res. Sect A* vol. 353, pp. 312-315, 1994.

[2] M. J. Paulus, et al "High resolution x-ray computed tomography," *Neoplasia* , vol 2, pp. 62-70, 2000.

[3] D. Strickland and G. Mourou "Compression of amplified chirped optical pulse." *Opt. Commun,* vol. 56, pp. 219, 1985.

[4] J. C. Kieffer, Z. Jiang, A. Ikhlef, C. Y. Cote, and O. Peyrusse, “Picosecond dynamics of a hot solid-density plasma,” *J.Opt. Soc. Am*. vol. B13(1), pp.132-137 (1996).

[5] O. Albert et al., *Opt. Lett*., vol. 25, pp. 1125, 2000.

[6] L. Grodzins, “Optimum energies for x-ray transmission tomography of small samples,” *Nucl. Instr. Methods*, vol 206, pp. 541-545, 1983.

[7] P. Spanne P, “X-ray energy optimization in computed tomography,” *Phys. Med. Biol*. Vol. 34, pp. 679-690, 1989.

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