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14. ABSTRACT
A new, compact, "tabletop" laser synchrotron X-ray device has been developed. It produces pulsed, tunable, monochromatic X-rays in 8-10 ps bursts. These X-rays emanate from the unit in a conebeam geometry from an effective focal spot of 50 microns. . The X-rays produced are tunable from 12-50 keV with each "shot" delivering 10^{10} photons. The unit utilizes a linear accelerator running in the single pulse mode and a tabletop terawatt laser integrated in such a way, that the X-rays are produced using the phenomenon of inverse Compton scattering. This device is used in a shirtsleeves environment, without the need for a shielded vault. The electron beam and laser beam are counterpropagated in a head-on collision yielding the tunable X-ray photons. The prototype unit has been designed, built and commissioned at the W.M. Keck Free Electron Laser Facility at Vanderbilt University, where it is now used for imaging animals, phantoms, and tissue specimens. A 1.5-meter long protein crystallography beamline has been designed and built for elucidation of 3-dimensional structures of protein crystals. This beamline is to be mated to an even smaller second-generation machine in a proteomics laboratory at the same MFEL facility.

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Final Technical Report for ONR Research Grant # N00014-99-1-0904

Principal Investigator: Frank Carroll, M.D.
Institution: Vanderbilt University Medical Center
Grant Title: Development of a Tunable, Monochromatic X-ray Device with the addition of a Beamline for Protein Crystallography at the Vanderbilt MFEL Facility.

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Technical Report:

Background: Delivery of high peak brightness, hard, tunable, monochromatic X-rays in an area geometry suitable and practical for rapid human imaging has been a long sought after goal. Few physical processes lend themselves to production of such beams as well as the phenomenon of inverse Compton scattering. While monochromatic X-rays have long been available at synchrotron facilities, they are largely inaccessible to the general patient population, since synchrotrons are not built around or in hospitals and clinics. The many impractical aspects of these light sources that make them less than ideal devices for diagnosis and treatment of everyday human maladies include (among others): exceptionally high costs, poor beam geometry, lengthy data acquisitions, and slow tunability. A device to produce X-rays in a clinical setting should be relatively compact and capable of delivering energies that encompass the useful diagnostic range. A practical source should be capable of delivering cone-beam geometry, with single shot imaging, over a broadly tunable range at variable bandwidth. If narrow bandwidth X-rays can be tuned to the task at hand, one can use quite different energies for monochromatic mammography versus chest or skull imaging. By using only the frequencies best suited to the examination being performed on a patient, one eliminates a significant portion of the radiation dose delivered to that person.

Synchrotrons are also widely used for the elucidation of the three-dimensional structure of a broad range of proteins. Since only six synchrotrons exist in the US, and the logistics of studying proteins at these facilities has become problematic for many, the development of a compact, tabletop synchrotron light source becomes an attractive goal.

Additionally, picosecond pulses also become valuable when studying physical, chemical or mechanical processes that occur on the planned X-ray beam's picosecond time scale. This may prove valuable for X-ray imaging in industrial processes, such as freezing and analyzing individual turbine blade assemblies in fully operational turbine or rocket engines, which are under full load, speed and temperature. Explosive processes, studies of armor failure modes when struck by high energy kinetic weapons, probing of individual features of radiation/EMP hardened microchips from reconnaissance, weather and navigational satellites, while under full power, and elucidation of crystallization in weld melts are only a few of the industrial uses anticipated at this time.

Objective: To develop a source of picosecond pulsed, tunable, monochromatic x-rays using an RF accelerator and terawatt laser for use in medical imaging and treatment, and to extend the use of this machine to performance of protein crystallography, and military/industrial applications.

The process: Inverse Compton scattering basically consists of the head-on collision of an energetic electron beam (traveling at a speed near the speed of light) with an intense beam of light, (in this case infrared (IR) light), each focused to an exceptionally small spot size at the point of collision. Light scatters off of the electrons, picking up some of the electron's energy and is deflected back out of the interaction zone (IZ) as an X-ray photon along an axis almost collinear with the direction of the electron beam's travel.

Approach: The electron beam from an RF linac is used to scatter infrared beams from a terawatt laser using the phenomenon of inverse Compton scattering to produce beams of pulsed, tunable, monochromatic x-rays. These x-rays are in the hard x-ray range from 12 to 50 keV (fundamental) with the capability of easily reaching hundreds of keV. The X-rays are focused into a small focal spot for protein crystallography, and are either collimated or allowed to diverge for use in human imaging and small animal imaging.

Accomplishments:

The machine: The system, which has been constructed and is now in use at the Vanderbilt MFEL facility, consists of the following basic subcomponents:

1. A master timing oscillator which provides the 81.6 MHz laser-mode-locking signal and the 2856 MHz master RF drive;
2. A timing monitoring and feedback system which monitors and corrects for timing drift due to transit time of signals through the laser and RF system, allowing few-ps timing consistency throughout the system;
3. A 200 fs Ti: Sapphire seed laser[1] running at 1052 nm and driving a stretcher/regenerative amplifier combination[2] which produces a 480 Hz train of 200 μJ pulses stretched to about 1 ns;
4. A Nd: YLF laser, pulse compressor and frequency quadrupler which provides up to 200 μJ of 263 nm light in 5 ps pulses for photocathode drive;
5. A Nd: glass laser[3] and pulse compressor, providing up to 10 J of 1052 nm light to collide with the electron beam;
6. An RF drive system and bare copper photocathode electron gun/LINAC to produce a high brightness electron beam, based on the Brookhaven ATF electron gun system and with similar electron beam characteristics[4];
7. A superconducting solenoid focusing magnet;
8. An interaction zone (IZ) and beam alignment system, where the electron beam and photon beam collide head on in a 50 μm spot; and
9. A beryllium exit window allowing the X-rays out of the vacuum beamline into the experimental area.

Some components of this hardware deserve more detailed commentary here, since they have been specifically designed to make this system robust and stable for daily operation. Because this facility will become an open user facility, extra efforts have been taken in the design to reduce instability in the system due to environmental changes and parameter drift.

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[1] Spectra Physics Tsunami

[2] Positive Light Spitfire

[3] Also built by Positive Light

[4] AES, Medford, NY

Item 2 in the above list is particularly critical to the system. The transit time of an optical pulse from the seed laser to the interaction zone is close to 1 μs, and needs to be stable to about 2 ps. Air, with an index of refraction of roughly n-1 = 3×10^{-4} contributes a 3 ps delay for each 1% change in atmospheric pressure. Also, small changes in the pressure of the fill gas in the waveguides, and small changes in the temperature of the electron gun can change the phase of the electric field in the gun, resulting in energy shifts in the electron beam. To avoid having to develop heroic environmental controls for the system, we have opted instead to monitor these timing variations and correct for them dynamically. This is done using a set of phase comparators which monitor the various timing offsets referred back to the master oscillator. This end-to-end timing monitoring system allows the system to remain extremely stable with very little effort or complexity.

The electron gun in item 6 has also been slightly adapted from the ATF design to make it more robust, at the expense of high photocathode drive laser energy being necessary. The modern trend in electron guns is often to pick high-quantum-efficiency materials for the photocathode to minimize the required laser drive. Unfortunately, most such materials, such as magnesium, form oxide layers, and need to be cleaned via laser ablation to maintain optimum performance. Instead, this machine uses bare, polished copper with no intentional laser cleaning. The operating vacuum in the gun is reasonably good (~ 3×10^{-7} Pa), and so the copper may slowly clean itself under the normal laser irradiation, but it is assumed that effectively the machine uses a copper-oxide cathode surface. Using a laser energy of about 100–200 μJ gives an electron pulse with a charge of 1 nC, which is what is needed to operate the machine. Under these conditions, the cathode never needs any reprocessing to maintain sufficient emission, which saves a good deal of time and effort.

Schematic of the device:

Figure 1 shows a general schematic of the system. Note the scale bar: the system is quite compact. Figure 2 shows a photograph of the system in its current configuration. On the left is the large Nd: glass laser. In the center, the long blue section is the lead shielding over the LINAC section. To the left rear is the seed laser table. The vertical blue tank is the superconducting solenoid, and the pulse compressor is to the right.

The actual photon yield of the system is variable and depends upon the considerations above and the actual beam quality and alignment, which are adjustable. We have not yet measured the absolute output flux of the system directly to high accuracy, as this requires very careful consideration, especially due to the extremely high-speed pulsed nature of the beam and the measurement devices that are currently available. This is also due to the fact that there is a background of high energy photons from stray electrons in the electron beam mixed with the Compton backscattered photons which need to be discriminated against. We are, therefore, in the process of verifying the metrology. However, as will be seen below, there is sufficient photon flux in any single 10 ps pulse to produce high-quality X-ray images, which is the first interest with this machine.

Imaging with the device:

Images have been made using various phantoms including a human hand phantom consisting of a preserved human hand skeleton embedded in approximately tissue-equivalent plastic, multiple breast phantoms, contrast agent phantoms, cell buttons and whole animals. Each image is performed using a single 10 ps pulse of X-rays.

Film/screen combinations currently in use in standard X-ray imaging are not a good match to the beam due to the extremely high speed of the X-ray pulse. For these preliminary imaging experiments, several detectors have been used including: a one inch diameter detector was used which incorporates components that are considered as proprietary information by the company supplying it, but it can be stated that the system uses a fluorescent image plate, coupled to an image intensifier, a tapered fiber optic bundle and a CCD camera[5]; a protein crystallography (CR plate); and an amorphous selenium on TFT array detector. Because the beam is not collimated for these images, the X-ray energy spectrum is slightly variable across these images, with the highest energy photons in the center of the beam and varying over the bandwidth of the beam at the time of imaging. In this case this was a 1% bandwidth.

As an example of the operation of this machine, images produced with it are presented in Figure 3. Since the energy of the electron beam can be varied over a range of 20-50 MeV, the energy of the X-rays produced is tunable. Figures 3A and B clearly show the difference between two different energies. At 19 keV the finger of the phantom shows good soft tissue detail, while the bone is radiopaque. At 26 keV, the bone becomes X-ray transparent revealing the cortex and medullary cavity within the bone, while the soft tissues become less distinct. To re-tune the machine from the lower energy to the higher energy, currently requires about 10 minutes of operator time, but this could be reduced to a few tens of seconds with computer-based saving and recalling of the few parameters required to make the adjustment.

Figures 3C and D show the differences visible with plane geometry imaging of a custom made conical breast phantom containing various elements of breast equivalent material embedded in paraffin. Arrows point to "lesions" easily seen with monochromatic X-rays that are practically invisible using standard polychromatic beams.

Figures 3E and F are low-resolution images of a whole mouse only slightly larger than one's finger. Sixty such images at various angles 3 degrees apart over 180 degrees are reconstructed into CT images for viewing in a standard computerized tomography format.

Protein crystallography:

A new beamline for use in protein crystallography has been built. Focusing the tunable monochromatic beam with multilayered X-ray optics and coupling this to a cryostat and crystallography camera allows the collection of crystallographic data similar to that obtainable at synchrotrons. This beamline is being tested on the current prototype machine with the plan of moving it to a new high rep rate machine designed and built just for protein crystallography and small animal imaging at the MFEL facility at Vanderbilt.

Beamline design was refined in conjunction with advice from external consultants at both national laboratory crystallography beamlines and private industrial users of X-ray crystallography. The output of the tunable, monochromatic machine (which has an effective focal spot of approximately 50 μ is focused on the protein crystal using a MaXFlux® multicoated X-ray optic. A MAR345® CR plate area detector and a 3 axis goniometer have been mated to an Oxford Cryostream® device and data acquisition computer running a Linux operating system. This new X-ray device and the MAR345 device have demonstrated sufficient sensitivity and coupling with the picosecond beam to deliver tunable, hard X-ray fluxes that are one to two orders of magnitude less than that available at a synchrotron source. Typically, however,

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[5] Nanocrystal Technology, Inc. Briarcliff, NY

synchrotron beams are attenuated to reduce flux delivered to the protein crystal to reduce degradation in the crystal during study. While the current high peak power, tunable, monochromatic machine delivers 10^{10} photons/8 ps shot of 12 to 50 keV X-rays with a 1-10% bandwidth at 0.01 Hz, the high rep rate machine now under development with MXISystems, Inc.[6], will deliver 8-15 keV X-rays at the rate of 10^{10} photons/sec with a similar bandwidth, but running at 30 Hz.

The completed protein crystallography beamline measures only 1.5 meters in length.

Commercialization of the device:

With matching funds from Vanderbilt University, a new startup company, MXISystems, Inc, constructed the new X-ray device at the W.M. Keck Free Electron Laser Center at Vanderbilt. This company was incorporated to commercialize this device, thereby transferring this technology into the commercial sector for use in protein crystallography, medical imaging and military/industrial non-destructive testing. Vanderbilt maintains the intellectual property on this device, and MXISystems, Inc. has negotiated exclusive rights to the patents mentioned below.

Publications:

1. Paschal CB, Carroll FE, Worrell JA, et al. Volumetric monochromatic X-ray tomography of the lungs. In: Edwards G, Sutherland JC, eds. Biomedical applications of free-electron lasers, vol. 3925, 2-7. SPIEE, 2000.
2. Carroll FE. Perspective. Tunable, Monochromatic X-rays: A New Paradigm in Medicine. AJR: 179, 583-590, 2002.
3. Carroll FE, Mendenhall MH, Traeger RH, Brau C, Waters JW. Pulsed, Tunable, Monochromatic X-rays from a Compact Source: New Opportunities. Submitted to American Journal of Roentgenology.
4. Edwards G, Carroll FE, et al. FEL Based Biophysical and Biomedical Instrumentation. Review of Sci Instr, in press.

Disclosures and Patents:

1. Carroll. Apparatus and Method for Three-Dimensional Imaging Using a Stationary Monochromatic X-ray Beam. U S Patent # 6,327,335 B1 Dated Dec. 04, 2001.
2. Carroll, et al. System and Method for Producing Pulsed Monochromatic X-rays. U S Patent # 6,332,017 B1 Dated Dec. 18, 2001.
3. Mendenhall, et al. Phase stabilizer. 2002. Patent Disclosure.

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[6] MXISystems, Inc., Nashville, TN

Figures:

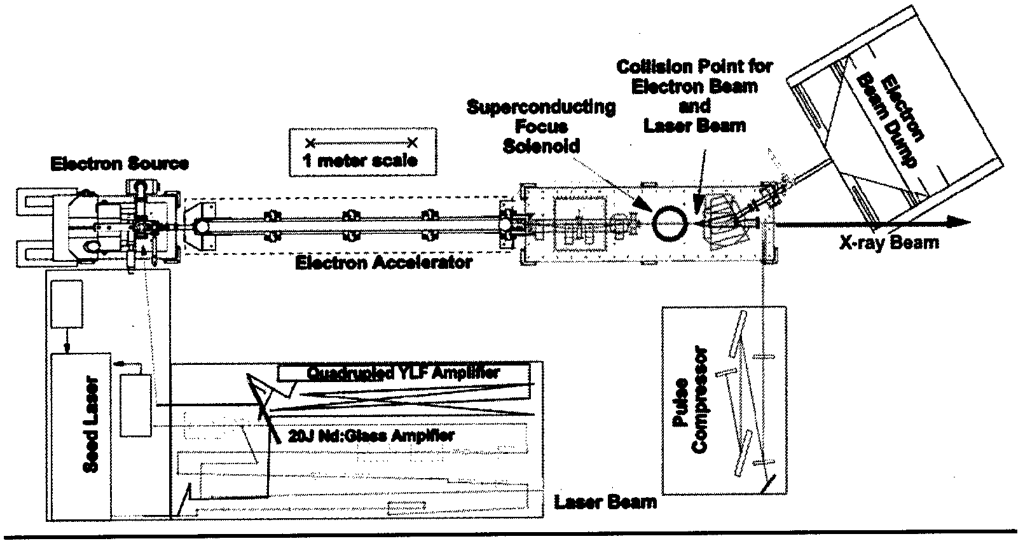

Figure 1 - Schematic of the machine.

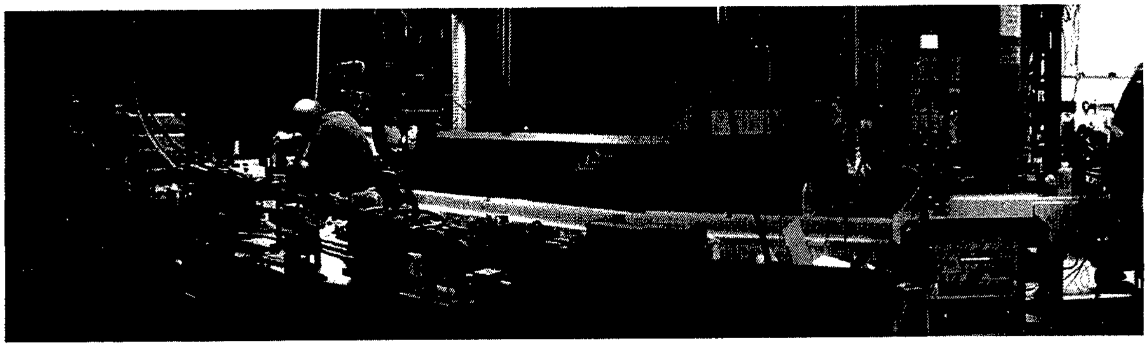

Figure 2 - Photograph of the device with the laser cover removed. Blue structure in the background is the accelerator. The laser is in the foreground.

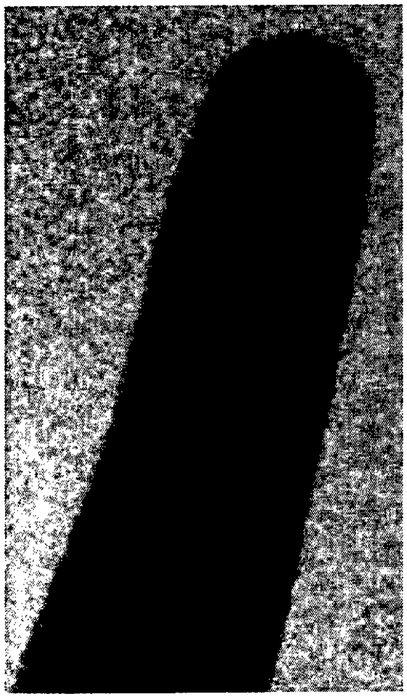

Figure 3A- A finger at 19 keV.
One cannot see through the bone.

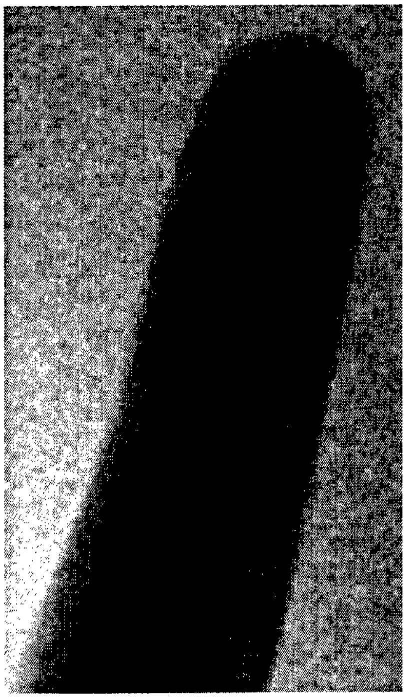

Figure 3B- Same finger at 26 keV.
Internal bone structures clearly visible.

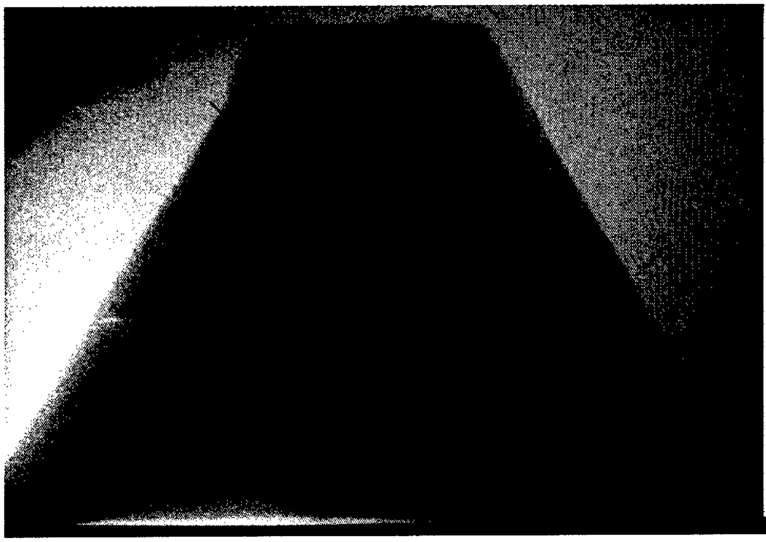

Figure 3C

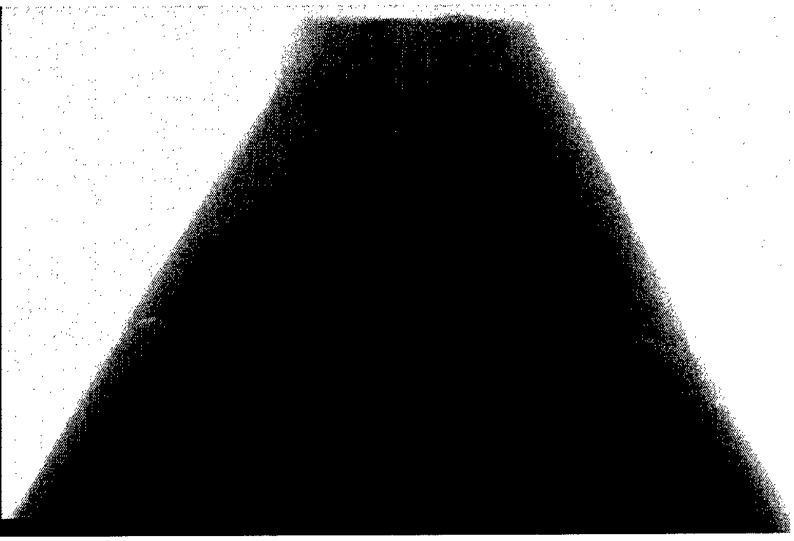

Figure 3D

Figure 3C shows the cone-shaped breast phantom imaged with a single 8 ps pulse of monochromatic X-rays. Many "lesions" (arrows) are visible in 3C, which cannot be discerned in 3D, which is an image of the same phantom taken with a polychromatic X-ray beam.

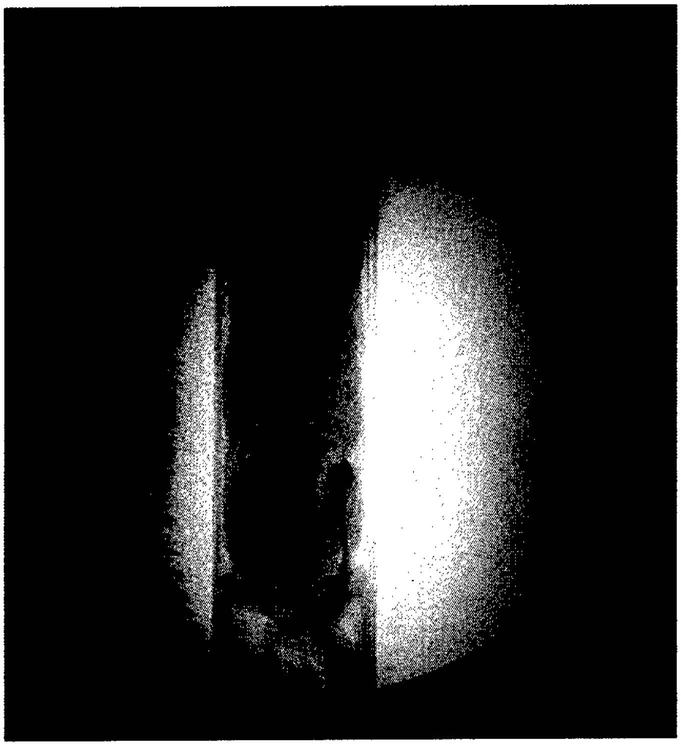

Figure 3E - Monochromatic X-ray of whole mouse.

Figure 3F- Low resolution of mouse's pelvis.