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3D Micro-CT for Functional Genomics

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Physics (CT: Technical Developments)

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Computer Code: G01 • 1½ hours

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High Spatial Resolution 3D X-ray Cone-Beam Microtomography

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PURPOSE: To develop a microtomography scanner for 3D in-vitro scanning of soft tissue and bone samples.

METHOD AND MATERIALS: A cone beam microtomography imaging system with variable magnification has been developed. The system components are: - a microfocus X-ray tube with transmission target, <5µm focus diameter, 0-100kV anode voltage, and 3W output power - a 2D CCD square detector with 1024^2 elements of $(19\mu m)^2$ size each, 3:1 magnifying fiber-optic taper, phosphor plate, Peltier cooling and 16 bit dynamic range - a flexible positioning system - software for raw data volume reconstruction, simulation, and image analysis The scanner exploits the advantages of cone beam geometry. The object and the detector can be independently translated with respect to the tube with a maximum tube-detector distance of 1000mm providing a maximum object image magnification of 20:1. The smallest voxel size is 2.5µm and the maximum object diameter is 50mm. Positioning stages allow for acquiring data using circular and complex trajectories, including spiral cone-beam and a combination of rotation and translation. For volume reconstruction approximate and accurate algorithms can be used. A variety of samples has been scanned, the tube focal spot stability has been measured, and sample alignment requirements have been determined.

RESULTS: - Acquisiton times of approx. 3h (10s exposure time, 720 projections) are sufficient for high contrast objects. Longer times are required for low contrast objects. - A spatial resolution of 10µm has been achieved (determined by thin tungsten wire phantoms). This requires the determination of the misalignment of the axis of rotation with very high accuracy (tilt $\leq 0.1^0$ and center-of-rotation shift ≤1µm). Correction can be done either by mechanical realignment or inclusion of the misalignment coefficients in the reconstruction algorithm. - Reconstruction using Feldkamp algorithm takes ≈2h for a 512^3 volume reconstructed from 720 projections on a Pentium III computer. - Measurements of the tube focal spot properties (using thin wire method) have been performed, and ≤5µm focal spot position stability has been found.

CONCLUSIONS: - A spatial resolution of a few micrometers is achievable, but requires very thorough scanner mechanical alignment. - A small focal spot size of the X-ray tube is essential, though not sufficient to achieve a high spatial resolution. Critical is also focal spot position stability during scan. Misalignment of axis of rotation due to this instability remains the main limitation for spatial resolution and cannot be easily corrected for.

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3D Micro-CT for Functional Genomics

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PURPOSE: With the sequencing of the human genome nearing completion, emphasis is being brought to bear on research methodology and appropriate technology to reliably and rapidly quantify phenotypes in genetically-engineered mice and other animal models relevant to human disease. These methods should be nondestructive and preferably noninvasive, low-cost and capable of high throughput.

METHOD AND MATERIALS: We have developed a special purpose micro-CT scanner capable of imaging objects ranging from one millimeter to several centimeters in size, including small animals and excised organs. Conebeam reconstruction algorithms are employed to directly reconstruct 3D image volumes from uncollimated 2D projection images acquired from many angles around the object using an image intensifier/CCD camera imaging chain. Analysis software was developed to extract dimensional and other measurements from the imaged volumes in a semiautomated fashion.

RESULTS: We have analyzed images of excised mouse, rat and dog lungs, dog hearts and of live anesthetized mice, with emphasis on contrast-enhanced arterial tree structures. Seeded 3D region growing techniques were used to segment vascular structures, with the imposition of connectivity constraints to preserve tree topology. Segment lengths and diameters were measured by interactive and semiautomated methods. Morphometric parameters derivable from the quantitative image metrics were sensitive to interspecies differences in arterial tree structures.

CONCLUSIONS: Imaging provides a class of methods to noninvasively extract phenotypes relevant to complex manifestations of gene expression. Automation of segmentation, feature extraction and classification algorithms remains a challenge, important for achieving the throughput and low costs required for more widespread application. Ongoing studies will assess the sensitivity of the method to vascular pathologies. Augmentation of the high-resolution structural information provided by transmission CT with the insights into functions like metabolism, elimination and messenger systems provided with exquisite sensitivity by emission CT would expand the power and applicability of tomography to functional genomics.

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3D Acetabular Models: Accuracy and Reliability of CT, Volume Rendering, CAD Modeling, and Rapid Prototyping

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PURPOSE: CT-based 3D volume rendering, CAD modeling and rapid prototyping (RP) realistically depict acetabular morphology and have potential to assist preoperative planning of complex surgeries. We sought to validate the accuracy and reliability of these techniques for depicting acetabular morphology with and without unilateral total hip prostheses in place.

METHOD AND MATERIALS: Spherical fiducial markers were placed on hemipelvi of three cadavers. Spiral (helical) and conventional CT were performed prior to and following insertion of unilateral total hip replacements. 3D volume renderings, CAD and RP models were created from CT image sets obtained at 2 different times. Accuracy and reliability were calculated by comparing repeated measures of direct (caliper) interfiducial marker measurements with repeated measures made from CT, volume renderings, CAD and RP models.

RESULTS: CT, volume rendering, CAD modeling, and rapid prototyping were accurate and reliable, with and without unilateral hip prostheses present. CT and 3D visualization and modeling methods, as compared to direct caliper measurements, underestimated caliper measurements by less than 1 mm. Test-retest reliability for CT and 3D methods was excellent, averaging 0.5 mm.

CONCLUSIONS: CT may be used to create accurate and reliable 3D volume renderings or CAD and rapid prototyping models of the acetabulum, even in the presence of unilateral total hip replacements.

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Development of a Subject-standing-type Cone-Beam CT for Chest and Orthopedic Imaging

(FDA)

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PURPOSE: A new 3D-imaging modality for subjects sitting or standing naturally is desirable especially for chest and orthopedic imaging. Cone-beam CT can acquire a full set of projection images during a single rotation scan and reconstructs an isotropic high-spatial-resolution 3D image. Our purpose is to develop a subject-standing-type cone-beam CT with high spatial resolution and a high S/N ratio.

METHOD AND MATERIALS: The developed system includes a turntable having a backrest. The subject may stand against the backrest, or can sit on chair placed on the turntable. The x-ray tube and the imaging detector are adjusted according to the subject imaging position and remain stationary during the scan. The detector consists of a 16-inch x-ray image-intensifier CCD camera. The camera acquires a 12-bit 512^2-pixel projection at 60 f/s, the rotation period is 4.8 s for 288 projections and 9.6 s for 576 projections. To reduce image noise, the system controls the x-ray-pulse duration and iris-opening area for each projection through real-time analysis of the projection image: pulse duration is controlled for subject transmittance compensation, and the opening area adjusts the light level to suit the CCD camera. To improve CT-value accuracy and eliminate artifacts, the veiling glare of the image intensifier and scattered x-rays are corrected by a newly developed method: blur-image components of glare and scatter are estimated and subtracted from each projection image. Human chest and orthopedic studies with 24 patients were conducted.

RESULTS: 3D images with sphere field of view (FOV) with a diameter of 21-25cm, 0.4- to 0.5-mm voxels, and a 512^3 matrix were obtained. During one rotation scan of geniculum, the typical x-ray exposure varied in the range of 1.8-4.4 ms depending on the imaging direction, which enabled high image quality at a low dose (30 mAs). In coronal, sagittal, and volume rendering images, the surface of arthrosis was visualized smoothly with a higher resolution than with conventional CT. In the case of gonarthrosis, narrowing of the clearance at the surface of arthrosis, an abnormal turn of patella, and dislocation of the thigh were visualized clearly; these abnor-