Assessment of a new CT system for small animals

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***Abstract*– We have developed an X-ray cone beam tomograph for in vivo small-animal imaging using a flat panel detector (CMOS technology with a columnar CsI scintillator plate) and a microfocus X-ray source in a geometric configuration with 1.6 magnification and 7.5 cm2 field of view. This work presents an initial characterization of this new system. We measured the detector modulation transfer function (MTF), detector stability, system resolution, the quality of the reconstructed tomographic images and radiated dose. The system resolution was measured following the standard test method ASTM E1696-95. For image quality evaluation, we assessed signal to noise ratio (SNR) and contrast to noise ratio (CNR) with respect to radiated dose. Measurements have been performed on Hounsfield-calibrated images of quantitative phantoms. Effective dose studies have been performed introducing TLD dosimeters in representative organs (ICRU criteria) of euthanized laboratory rats for different imaging protocols. Noise measurements indicate that 50 HU can be achieved at a dose of 10 cGy. Effective dose in standard research methods is below 200 mSv, confirming that the system is appropriate for in vivo imaging. Maximum spatial resolution achieved is better than 50 microns. Experimental results on image quality phantoms as well as on in-vivo studies show that the use of CMOS flat panel is a good choice in terms of quality with respect to radiated dose.**

I. Introduction

X-ray micro computed tomography based on a flat-panel and a cone-beam geometry has rapidly developed in the last two decades. This configuration presents great advantages over classical techniques in clinical and preclinical applications: Reduction of acquisition time, large axial field of view and optimization of radiated dose per time and data acquired. Additionally, physical characteristics of flat panels are particularly appropriate for small animal imaging due to it high resolution capability [1].

We developed a new micro-CT system made up of a flat panel (CMOS technology with a columnar CsI scintillator plate) with a pixel size of 50 microns and a microfocus x-ray source (35 microns of focal spot size). Both elements are placed in a common rotating gantry conforming a circular cone-beam geometry. Distances between the elements were designed for a 7.5 cm2 field of view and 1.6 magnification factor.

In this work, system characteristics have been evaluated in a standard way to compare it with previous systems and to validate its use for *in-vivo* imaging. The design aims for the present system were a field of view appropriate for small rodents, a spatial resolution better than 50 microns and to minimize radiated dose.

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II. Methods and materials

A. CMOS detector evaluation

Performance of the detector was evaluated in terms of stability and MTF: stability affects tomographic images by increasing noise and artefacts; MTF represents the intrinsic resolution of the detector and determines the final resolution that the system can achieve.

To test the detector stability, 360 consecutively flood images without any object between source and detector were acquired with the X-rays source set to 30 KV and 0.4mA. The images were acquired after waiting 10 seconds to stabilize the source photon flux. The mean pixel value was measured for each image.

The Modulation Transfer Function (MTF) due to the detector was calculated by direct analysis of the edge response function (ERF). The ERF was obtained from an image of an X-ray opaque object with a polished edge. ERF was adjusted to an integrated Gaussian function, as described in [2]. Point spread function (PSF) is the analytical first derivative of the ERF and MTF was obtained taking the Fourier transform of the PSF. Following this method, the detector intrinsic MTF was obtained by placing the object close to the detector (no magnification), and the composed MTF, reflecting the combined effect of the detector and the finite focal spot size of the source [3] was obtained by imaging the object at nominal system magnification.

B. Reconstructed image quality evaluation

The evaluation of the reconstructed images was based on measuring Noise Level, Contrast to Noise Ratio (CNR) and spatial resolution, which constitute the main features in terms of image quality for preclinical applications.

Noise in reconstructed images was evaluated on a homogeneous water phantom by measuring the relative standard deviation of the signal (in Hounsfield Units), as a function of radiated dose. The phantom was acquired six times at 25 KV and $600\,\mu A$ at different doses (different number of averaged images for each angular position).

Contrast to Noise Rate (CNR) has been measured as a function of radiated dose using a contrast phantom which consists of a nylon cylinder (1.15 g/cm^3), immersed in a water tank (Fig. 1). CNR is defined as

$$CNR = \frac{|\mu_n - \mu_w|}{\sqrt{\sigma_n^2 + \sigma_w^2}}$$

Where μ and σ are the mean and standard deviation of the pixel values, respectively, in a given area of the water (μ_w, σ_w) and nylon (μ_n, σ_n) in the reconstructed images. ROI´s obtained by thresholding were used for the analysis.

The final resolution of the system was measured following the standard test method E1696-95 [4]. This method is based on the examination of the CT image of a uniform disk of polycarbonate (1.18 gr/cm^3) (Fig. 1).The measurement is derived from an analysis of the edge of the disk obtaining the ERF; the PSF is calculated by deriving analytically the ERF and, in turn, the MTF.

All the reconstructions were performed using a Feldkamps´s algorithm, filtering the projections with the Ram-Lak filter.

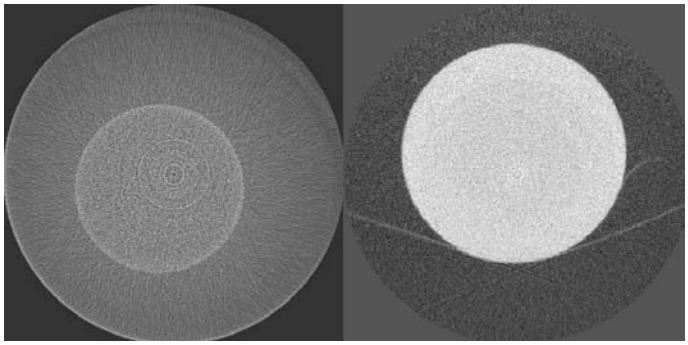

Fig. 1 Transaxial image of the nylon-water phantom used to measure CNR acquired with 5.3 cGy (left); transaxial image of the polycarbonate disk used to evaluate spatial resolution (right)

C. *Effective dosis evaluation*

To obtain a more precise assessment of biological effects in *in-vivo* studies than that offered by purely physical exposure measurements, we performed a study to estimate effective dose. In this kind of studies, real absorbed dose in tissues is measured and the biological importance of different tissues is taken into account.

The protocol consisted of the following steps: thermoluminescent dosimeters (STI, TLD-100) were introduced into representative tissues of euthanized rats, the rats underwent standard acquisition protocols and finally effective dose was estimated by , weighting the relative biological importance of the different tissues according to ICRU (International Commission for Radiological Units) criteria.

III. Results

A. *CMOS detector evaluation*

Detector stability is shown in Fig. 2, where a slight increase of the signal (<0.3%) can be observed. This result indicates that the CMOS detector is extremely stable.

Intrinsic resolution of the detector, defined as MTF 10%, resulted in 8.1 lpmm, compatible with manufacturer's specifications.

MTF 10% measured at nominal system magnification was 12.53 lpmm, almost 1.6 times intrinsic resolution. Considering how that both components, detector and source, affect the final resolution [3], the limiting factor in this configuration is the intrinsic resolution of the detector and the effect of the finite focal spot results almost negligible.

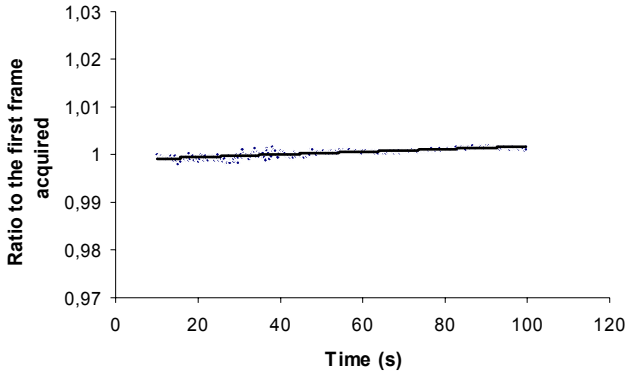

Fig. 2 Stability measurements, mean value (ratio to the first acquired frame) with respect to time.

B. *Reconstructed image quality evaluation*

Noise level decreases proportionally to square root of dose, as expected according to theoretical noise models for CT images [5]. A good soft tissue contrast is achieved for noise level below 50 HU, corresponding to a radiated dose of 7.5 cGy. Fig. 3 shows the results of noise level as a function of dose.

Fig. 4 shows a plot of the CNR with respect to radiated dose. It can be noticed that CNR increases proportionally to the square root of the dose. From the measurements, we can observe that the CNR obtained for a dose of 7.5 cGy is 0.98

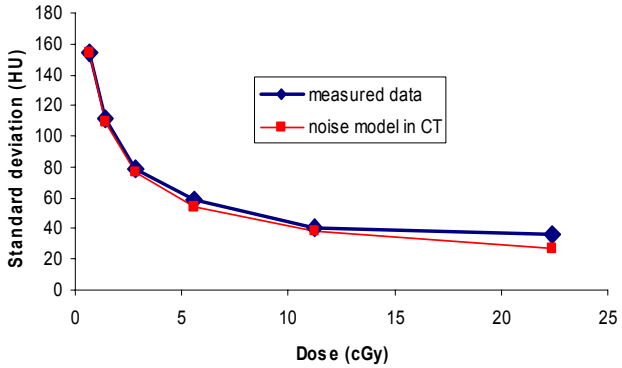

Fig. 3 Noise level (standard deviation) in Hounsfield Units as a function of radiated dose; measured data in blue and Gaussian model in red.

MTF 10% measured according to the standard protocol E1696-95 was 11.34 lpmm or 44 μm in the spatial domain. The observed actual resolution in reconstructed images is lower than the resolution measured in projection due to the reconstruction process and to possible submillimetric misalignments [6].

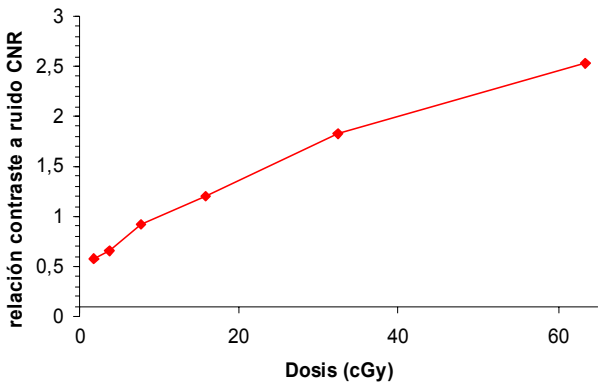

Fig. 4 Contrast to Noise Ratio (CNR) as a function of radiated dose.

C. *Effective dosis evaluation*

Table 1 shows the results and the acquisition settings for two standard protocols, the first one used to contribute with anatomical information in PET-CT studies and the second corresponding to a high resolution protocol for bone tissue. The effective doses obtained were, respectively, 0.5 % and 2% of LD50/30 (~7.5 Sv) for small rodents,

TABLE I
X-RAY SETTINGS AND EFFECTIVE DOSE FOR ACQUISITION PROTOCOLS

Voltage	Amperage	Time	Bed positions	Resolution	Effective dose
25 KV	600 µA	6´00"	2	200 µm	33,73 mSv
40 KV	750 µA	6´30	1	100 µm	165,2 mSv

IV. DISCUSSION AND CONCLUSION

Size of commercial CMOS detectors makes them suitable for small animal imaging; yielding a more compact design than that obtained with CCD detectors; the more common choice in this kind of systems.

We have shown that the CMOS flat panel detector offers good results in terms of noise, contrast and resolution. These features make it possible to optimize image quality in terms of radiated dose in the study.

The elements and the configuration of the system achieve a spatial resolution better than $50\,\mu m$, a basic design criterion. We characterized source and detector components of the resolution and how it is degraded in the reconstruction process. , As the limiting factor in this configuration is the detector, final resolution would benefit from using new versions of the flat panel with an intrinsic resolution of 10 lpmm, with no other change in the system.

Results of dosimetry show that the system is suitable for in-vivo imaging, especially when using relatively low resolution protocols ($200\,\mu m$). If the resolution is doubled for a given X-ray settings, voxel noise increases 4 times. For this reason, special care must be taken with X-ray settings for ultra high resolution protocols. Another consideration in effective dose calculation is that ICRU factors are estimated for humans, although they may be a reasonable approximation for murine models.

Several previous studies have been published [7-11] evaluating micro-CT systems, but the comparison between systems is difficult because of the different technologies involved. The lack of a standard methodology for the evaluation hinders even more this comparison.

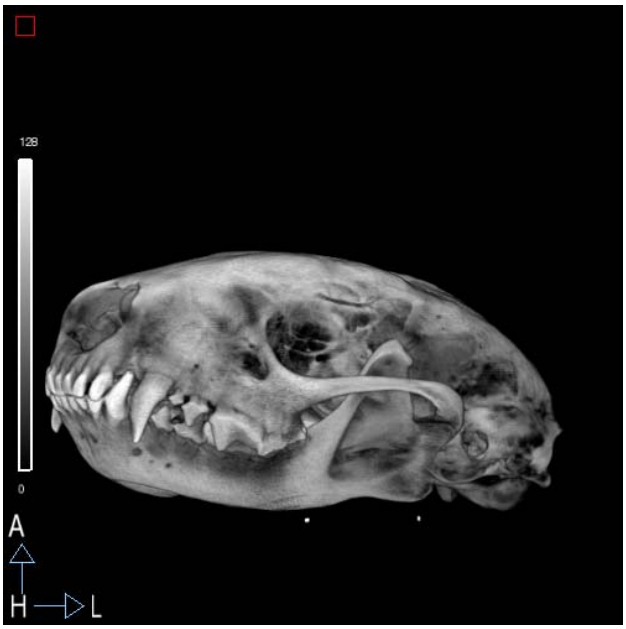

Fig. 5 Skunk skull volume rendering from FDK reconstructed volume of 512^3 voxels with a radiated dose of 3cGy in 1.5 minutes acquisition time.

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