Small Animal CT with Micro-, Flat-panel and Clinical Scanners: An Applicability Analysis

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ABSTRACT:

Over the past 30 years, X-ray computed tomography (CT) has developed into one of the most important imaging techniques for the examination of subject morphology to date by non-invasively offering images of anatomy with high spatial and low-contrast resolution. Of late, pre-clinical research has increasingly relied on the use of laboratory animals and the interest in small animal imaging has risen due to an increased availability of animal models of disease. While clinical multi-slice CT has been used for small animal imaging, scanner systems like micro- and flat-panel detector Volume-CT have come to the fore to meet the requirements of small animal imaging in pre-clinical studies by a down-scaling of clinical CT accounting for the difference in size between humans and small animals, e.g. by offering higher spatial resolution.

The overall goal of this thesis was to determine which technical concept of CT is best suited for addressing which problem of in-vivo small animal imaging. To this end, custom-designed small animal phantoms have been developed along with methods for an applicability analysis of different physical scanner concepts in view of in-vivo small animal CT imaging. Technical scanner concepts comprised clinical multi-slice CT (MSCT), flat-panel detector Volume-CT (fpVCT) and micro-CT (μCT). For these scanners the decisive parameters of small animal CT imaging, i.e. homogeneity, noise, temporal stability, CT number scaling, spatial resolution, low-contrast resolution and radiation exposure, have been studied in dependence of acquisition parameters (X-ray tube voltage, gantry rotation time, scan field-of-view (FOV), detector frame rate and readout binning (fpVCT only)) in a small animal phantom study. The phantom study results were tested in vivo with dynamic contrast-enhanced (DCE) scans. Data acquisition and analysis was based on large measurement statistics and conducted in a uniform manner for all three scanners.

The phantom studies show that CT number homogeneity of the clinical MSCT scanner is independent of gantry rotation time and almost independent of phantom diameter (±2.5 HU) as well as tube voltage (15 HU max. difference). Noise mainly depends on gantry rotation time and is low (4−14 HU). Temporal stability is ±(2−4) HU for a temporal resolution of 0.5 s. CT number scaling is non-linear due to beam hardening but can be calibrated to conform with the Hounsfield scale. Spatial resolution is limited by noise and in the order of 360 μm at

best; low-contrast features of ~1 mm can normally be detected. Depending on chosen tube voltage, whole body radiation exposure of small animals lies in the range of (70–230) mGy · cm (50 mA, 1 s). Acquisition parameters can be chosen such that exposure stays below the threshold of 100−300 mGy (e.g. 70 mGy · cm at 80 kV), an exceedance of which is believed to induce radiation effects. In-vivo DCE scanning yields stable results consistent with the phantom studies and allows to determine quantitative parameters, e.g. rat liver perfusion (according to the perfusion model of Miles) of (0.0752–0.0782) min^{-1} or liver blood flow of (0.72–0.75) ml/min.

Homogeneity measurements for the fpVCT scanner reveal small dependence on gantry rotation time (±(2−5) HU) but strong dependence on tube voltage or selected detector mode (up to ~180 HU difference). Cupping leads to differences between CT numbers measured centrally and in the periphery of 40 HU or 75 HU (objects of "mouse"- or "rat"-sized phantom cross-section, resp.). Noise solely depends on gantry rotation time and is 6 times higher than for MSCT. Temporal stability is ±(1−6) HU for reconstructed temporal resolution between 2−5 s. CT number scaling is also non-linear and cut off at +3071 HU, the linear scaling regime can be calibrated. Spatial resolution depends on gantry rotation time and detector mode: at best it is ~200 μm. Reliable detection of low-contrast lesions of ~1 mm is possible for longer gantry rotation times, e.g. ≥ 14 s at a tube voltage of 80 kV. Radiation exposure lies in the range of (100–980) mGy · cm (50 mA, 10 s) depending on chosen tube voltage; thus care must be taken to avoid excessive exposure. Results of in-vivo DCE scanning are stable (e.g. rat liver perfusion (Miles): (0.0346–0.0435) min^{-1} or liver blood flow: (0.33–0.42) ml/min) but precision is limited by low temporal resolution, especially if compared to MSCT.

The μCT scanner exhibits good CT number homogeneity (±1 HU) independent of gantry rotation time but slightly dependent on FOV size (3 HU) and strongly on tube voltage (+50 HU shift between 35 and 50 kV). Noise only depends on rotation time and reaches the worst MSCT noise level at best. Temporal stability is good (±1 HU), whereas temporal resolution is low with 4.5 s/rot. Non-linear CT number scaling is encountered which again can be calibrated by double-linear fitting. Spatial resolution is independent of tube voltage and rotation time but depends on FOV size and reaches 100 μm for the smallest FOV through geometric magnification. Low-contrast structures of ~1 mm can be resolved with medium reliability for long rotation times through implicit noise suppression. Small animal whole body radiation exposure can be as low as ~40−50 mGy · cm (50 kV, 4.5 s/rot., 58 slices) for fast scanning and low number of slices with large scan increment; it ranges from (40–440) mGy · cm depending on scan settings. In-vivo DCE scanning is possible for recording slow tissue enhancement dynamics; otherwise temporal resolution is too low.

According to the aforementioned findings clinical MSCT is best suited for quantification of DCE small animal studies because of its good homogeneity, low noise level, high temporal resolution and low-contrast resolution; spatial resolution is limited in view of small animal CT but of secondary importance in DCE studies. fpVCT offers increased spatial resolution and is thus suited for studies of small animals of the size of a rat; in addition, large volume coverage makes it an ideal choice for high throughput imaging and for gated scans requiring good volume coverage per rotation. However, its non-uniform behavior is a hindrance for quantitative studies. Highest spatial resolution in combination with a good overall stability of imaging parameters has been found for μCT; it should thus be employed for quantitative studies of small animal morphology for which high temporal resolution is not required.

In summary, the presented applicability analysis involving the three CT scanner designs most commonly employed for small animal CT imaging shows that no single scanner design is able to meet all imaging performance requests raised by small animal CT yet. Instead, a careful selection of a suitable scanner system depending on clinical problem is required. The applicability analysis subject of this thesis provides a scientific basis for the decision which scanner concept is most suited for addressing a specific problem of in-vivo small animal CT imaging.

Thesis-related journal publications:

[1] W. Stiller, M. Kobayashi, K. Koike, U. Stampfl, G. Richter, W. Semmler, F. Kiessling, "Initial experience with a novel low-dose micro-CT system / [Erste Erfahrungen mit einem neuen Niedrigdosis-Mikro-CT]," Rofo **179**, 669–676 (2007).

[2] S. H. Bartling*, W. Stiller*, W. Semmler, F. Kiessling, "Small animal computed tomography imaging," CMIR **3**, 45–59 (2007). *Equal contribution first authorship.

[3] S. H. Bartling, W. Stiller, M. Grasruck, B. Schmidt, P. Peschke, W. Semmler, F. Kiessling, "Retrospective motion-gating in small animal CT of mice and rats," Invest. Radiol. **42**, 704–714 (2007).

[4] S. H. Bartling, J. Dinkel, W. Stiller, M. Grasruck, I. Madisch, D. Trnka, H.-U. Kauczor, W. Semmler, R. Gupta, F. Kiessling, "Intrinsic respiratory gating in small animal CT," Eur. Radiol. **18**, 1375–1384 (2008).

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