Gerd Wolfram Stiller
Dr. sc. hum.

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

Geboren am 22.12.1976 in Kassel, Hessen, Deutschland
Diplom der Fachrichtung Physik am 13.12.2002 an der Ludwig-Maximilians Universität (LMU) München

Promotionsfach: DKFZ (Deutsches Krebsforschungszentrum)
Doktorvater: Prof. Dr. rer. nat. Dr. med. Wolfhard Semmler

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 MSCT 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, methods for and results of an applicability analysis of different physical scanner concepts in view of in-vivo small animal CT imaging are presented. These technical scanner concepts comprise clinical 16-slice MDCT, flat-panel detector Volume-CT and micro-CT. 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 with custom-designed small animal phantoms as well as in exemplary dynamic contrast-enhanced scans in vivo. Data acquisition and analysis was based on large measurement statistics and conducted in the exact same manner for all three scanners wherever possible.

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.). 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 could 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. With 70 mGy · cm (80 kV, 50 mA, 1 s) whole body radiation exposure of small animals lies below the threshold of 100 − 300 mGy 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 blood flow: 0.74 ml/min).

Homogeneity measurements for the VCT 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 ("mouse"- or "rat"-sized object, resp.). Noise solely depends on gantry rotation time and is 6× 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 could 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. Radiation exposure lies in the range of 100−900 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 but by far not as precise as for MSCT because of lower temporal resolution.

The micro-CT 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. Whereas temporal stability is good (±1 HU), with 4.5 s/rot. temporal resolution is low. Non-linear CT number scaling is encountered which again could 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 in 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 is ~ 40−50 HU (50 kV, 4.5 s/rot., 58 slices) for fast scanning and low number of slices with large scan increment. 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 dynamic 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. VCT 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 micro-CT which 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 main CT scanner designs 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. However, the results of the quantitative phantom studies investigating the key parameters of small animal CT as well as the results of the exemplary animal experiments presented in the applicability analysis at hand provide the solid scientific basis for the decision which scanner concept is most suited for addressing a specific problem of in-vivo small animal CT imaging which has thus far been lacking throughout all scientific work published on small animal CT imaging.