

In Vivo MRI of Rat Thyroid Glands for Non-Invasive Virtual Histopathology

B. Künnecke¹, B. Lenz¹, M. Stephan-Güldner¹, A. M. Brändli-Baiocco¹, J. Funk¹, T. Pfister¹, and M. von Kienlin¹

¹Pharmaceuticals Division, F. Hoffmann-La Roche Ltd, Basel, Switzerland

Background - Thyroid and parathyroid are two endocrine glands implicated in regulation of growth and metabolism as well as calcium homeostasis. Thyroid hypertrophy, hyperplasia and neoplasia are spontaneous findings often observed in rats in non-clinical safety studies. Such findings, however, can also be induced by investigational compounds. In order to understand the time of onset, progression and potential regression of these abnormalities longitudinal (i.e., time course) assessment are required. In humans, MRI is a well established non-invasive imaging modality to examine thyroid glands for neoplasias⁽¹⁻³⁾. In contrast, in vivo MRI of thyroids in rodents is not established and current literature is very scant⁽⁴⁾. The purpose of the present study was to back-translate this modality to the rodent model. Rat thyroid and parathyroid glands were assessed non-invasively by in vivo MRI and subsequently by conventional histology for comparison.

Methods - Naive old male Sprague-Dawley rats (n=34, age ~12 months) were used as a model of age-related spontaneous abnormalities. Freely breathing animals were anaesthetised with isoflurane in a mixture of N₂O/O₂ supplied via a face mask. MR images of the thyroid glands were acquired before and after intravenous injection of 187mg/kg GdDTPA (Magnevist, Bayer). In vivo MRI was carried out on a Bruker Biospec 4.7T/40cm instrument equipped with a transmit body resonator and a receive-only surface coil that covered the animals' throat. Sagittal scout images were obtained with a fast gradient-echo sequence and used for further scan planning. Transversal high-resolution images of the thyroid glands *in situ* were then acquired with a RARE sequence with TR/TE_{eff}=1530/33ms, 15 consecutive slices with 0.5mm thickness, a field-of-view of (35mm)², a data matrix of 256x256 points and 13 minutes scan time. After imaging, the animals were terminated and serial sections of the thyroid glands were histopathologically examined and compared with the MRI images.

Results and Discussion - In vivo MRI of thyroid glands elicits natural contrast from surrounding, mostly muscular tissue at the present acquisition conditions. Images acquired after GdDTPA administration reveal selectively enhanced parathyroid glands. Figure 1 depicts a magnified view of a transversal image taken from the neck region (see insert). The two lobes of the thyroid gland are located to the left and right of the trachea and are connected with a narrow bridge across the trachea's anterior belly. The arrows indicate the parathyroids, which constitute the lateral extensions of the thyroid gland. Most notable, GdDTPA also enhanced the contrast behaviour of thyroid lesions. In vivo MR images acquired five minutes after administration of GdDTPA identified different neoplasias as confirmed post mortem by classical histopathology. In particular, C-cell adenomas, which consist of densely packed small cells, showed as hyper-intense areas (Figure 2). On the other hand, cystic follicular cell adenomas appeared as hypo-intense regions (Figure 3).

Conclusions - The present study demonstrates successful back-translation of thyroid MRI from human to laboratory rodents. MRI yielded excellent tissue contrast in rat thyroid (and parathyroid) glands, thus providing the prerequisite for routine and repeated virtual histology of thyroid glands *in situ*. Comparison to histopathological sections revealed good correlation in terms of anatomy and tissue classification for lesions larger than approximately 500um in diameter whereas smaller lesions escaped unequivocal detection by MRI.

References

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