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Improving postoperative MR imaging of pituitary macroadenomas: comparison of full and reduced dose of gadopentetate dimeglumine

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Abstract. The aim of this study was to evaluate the efficacy of contrast-medium (CM)-enhanced MR imaging of operated pituitary macroadenomas with reduced dose of gadopentetate dimeglumine. In a prospective study 18 patients were examined with coronal T1-weighted MR imaging prior to and following intravenous CM injections. Two sets of contrast-enhanced coronal images were obtained in each patient; the first set after 50% of the recommended dose of 0.1 mmol/kg body weight (b.w.) had been administered, and the second set immediately after additional CM had been given to make up a total dose of 0.1 mmol/kg b.w. The images were evaluated by three neuroradiologists. The SIPAP classification system was used to evaluate tumour extension, whereas tumour margin conspicuity was scored using an arbitrary scale of 1–5 (1 = indistinct, 5 = well defined). Signal intensity measurements obtained from the most enhancing part of the adenomas demonstrated increased enhancement with increased CM dose. Tumour delineation scores were significantly better on the reduced- and full-dose images than on pre-CM injection images, but, with one exception, tumour extension was identified as the same on all imaging sequences. Postoperative MR imaging of large macroadenoma residues can routinely be performed without intravenous CM. When CM is indicated a reduced dose of gadopentetate dimeglumine should provide sufficient diagnostic information.

Key words: Magnetic resonance imaging – Contrast medium – Cost benefit – Surgically treated macroadenomas

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Introduction

Although contrast-medium (CM)-enhanced MR imaging is the gold standard for imaging a variety of lesions of the central nervous system [1], the optimal CM dose has yet to be decided [2, 3, 4, 5, 6]. Package inserts for Magnevist (gadopentetate dimeglumine, Schering, Berlin, Germany), recommend a dose range from 0.1 to 0.2 mmol/kg body weight (b.w.), whereas inserts for Omniscan (Gadodiamide injection, Nycomed, Oslo, Norway) and Prohance (Gadoteridol, Bristol-Myers Squibb, New York, N.Y.) recommend 0.1–0.3 mmol/kg b.w.

It has been reported that 0.1 mmol/kg b.w. is more effective at enhancing intracranial tumours than lower doses at mid- and high-field MR units [7]. Furthermore, it has been shown that high dose (0.3 mmol/kg b.w.) improved lesion detectability in patients with brain metastases, compared with low dose (0.1 mmol/kg b.w.) in the same patients [4]. However, it has been suggested that a reduction in CM dose from 0.1 to 0.05 mmol/kg b.w. is beneficial in the diagnosis of pituitary adenomas, and also that such CM dose reduction resulted in no significant diminution in post-CM-injection signal intensity in the normal pituitary gland or adjacent tissues [2, 8]. The need for further studies to clarify whether a dose reduction is affordable in the evaluation of extra-axial tumours, has been pointed out [9].

The purpose of this study was to evaluate the efficacy of CM-enhanced MR imaging of surgically treated pituitary macroadenomas with reduced dose of gadopentetate dimeglumine.

Subjects and methods

In a prospective study 18 consecutive patients with surgically treated macroadenoma were included. There were 10 men and 8 women aged 25–85 years (mean age 49.6 years). The MR examinations were performed on a 1.5-T Magnetom (Siemens, Erlangen, Germany). Us-

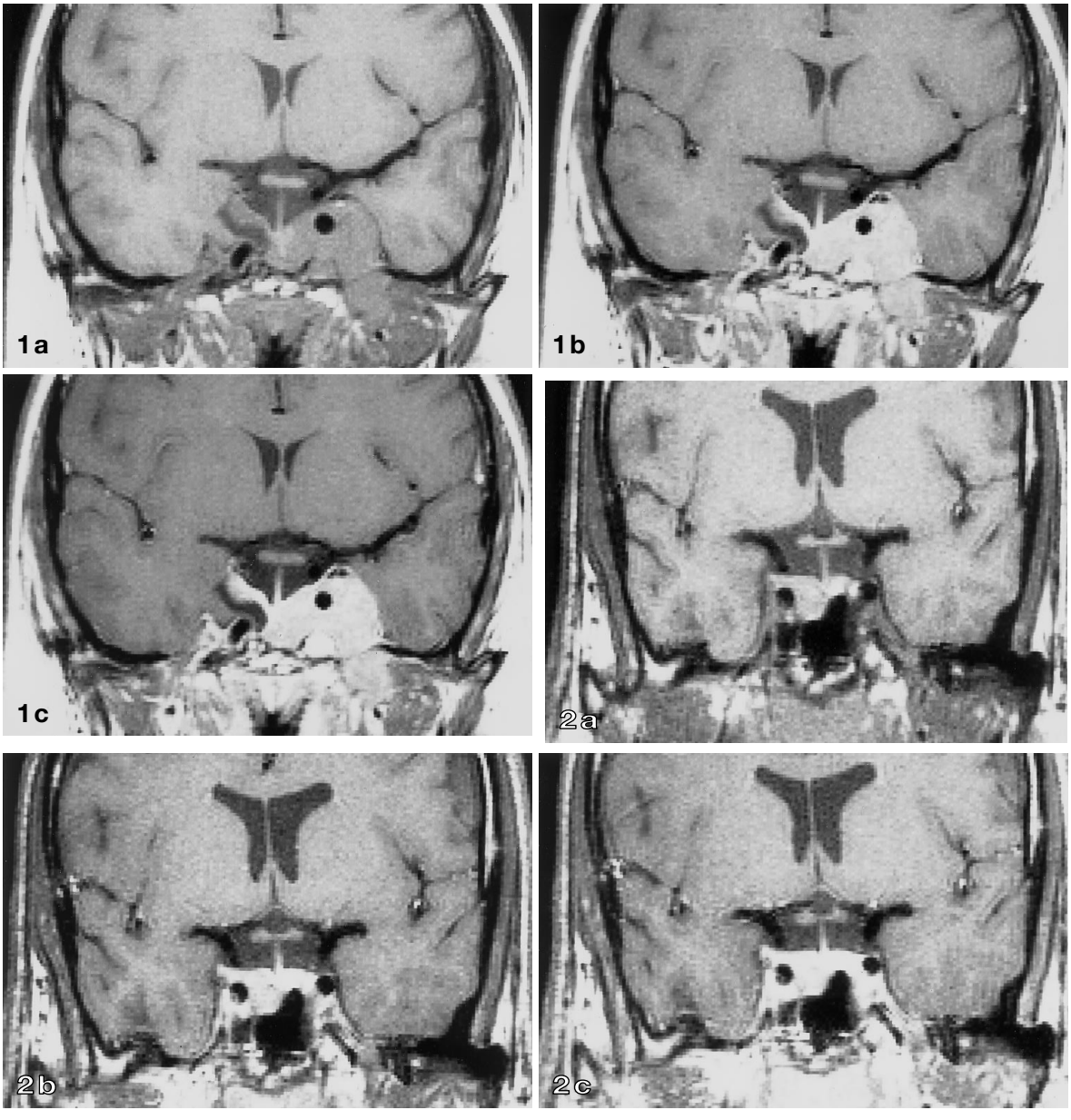

Fig. 1 a–c. Patient 2. Postoperative MR images demonstrate a macroadenoma infiltrating the left cavernous sinus and extending through the base of the skull. **a** Coronal T1-weighted image prior to contrast medium injection, **b** after administration of 50% of 0.1 mmol/kg b.w. of gadopentetate dimeglumine and **c** after additional gadopentetate dimeglumine to make up a total dose of 0.1 mmol/kg b.w. The tumour is well seen on all three images

Fig. 2 a–c. Patient 3. Coronal T1-weighted image **a** prior to contrast medium injection, **b** after administration of 50% of 0.1 mmol/kg b.w. of gadopentetate dimeglumine and **c** after additional gadopentetate dimeglumine to make up a total dose of 0.1 mmol/kg b.w. Images **b** and **c** demonstrate contrast medium enhancement of the pituitary stalk and gland, and better than the unenhanced study of **a**, they identify the interface between the residual macroadenoma and the pituitary gland. There is tumour infiltration of the right cavernous sinus

ing a head coil 3 mm thick T1-weighted images (T1WI; TR/TE = 600/20 ms), field of view (FOV) 230 × 230 mm, number of acquisitions = 4 and matrix 220 × 256 were obtained in the sagittal and coronal planes prior to CM injection and in the coronal plane following the intravenous injection of Magnevist (gadopentetate dimeglumine, Schering, Berlin, Germany). In each patient two sets of post-CM-injection images were obtained; the first set of images after 50% of the recommended dose of 0.1 mmol/kg b.w. had been administered, and the second set immediately after additional intravenous CM had been given to make up a total dose of 0.1 mmol/kg b.w. for each patient [10]. Each coronal imaging sequence had an acquisition time of 8 min 52 s. An intravenous line was established prior to imaging.

In each patient the pre- and post-CM injection coronal T1WI were compared with each other with respect to tumour detectability and tumour extension. All im-

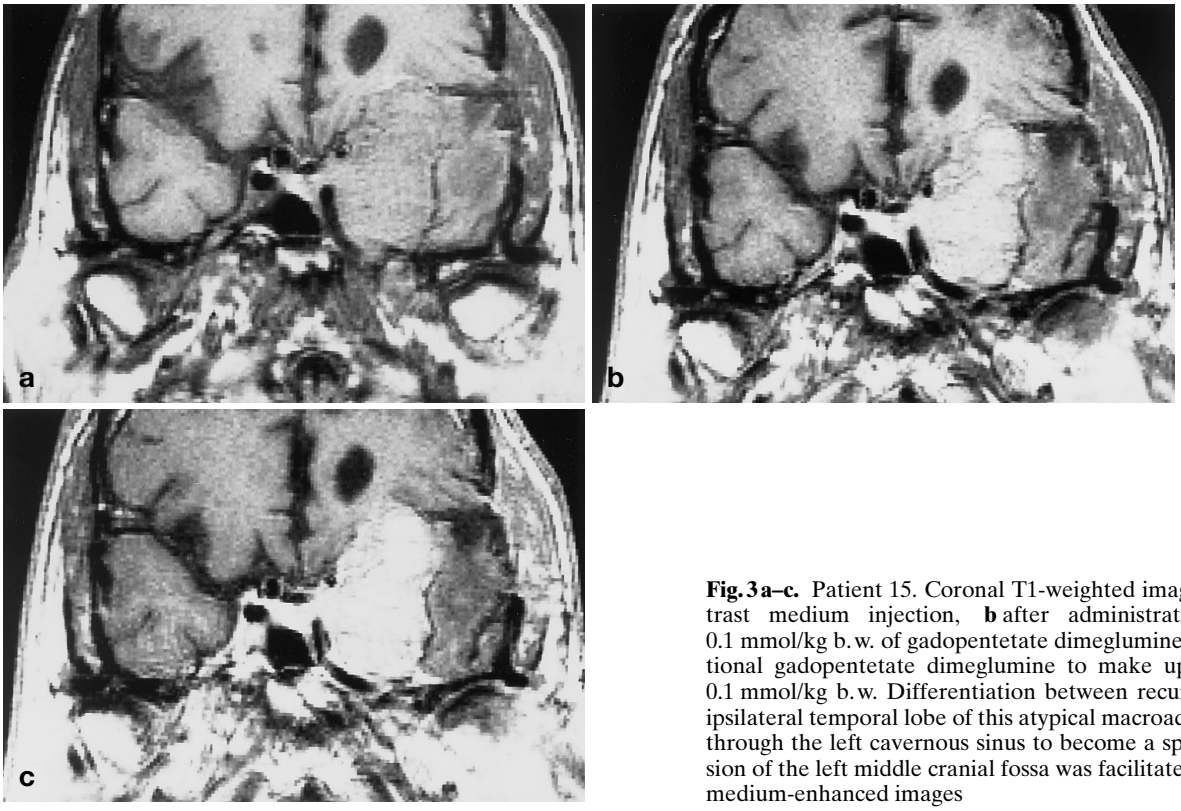

Fig. 3 a–c. Patient 15. Coronal T1-weighted image **a** prior to contrast medium injection, **b** after administration of 50% of 0.1 mmol/kg b.w. of gadopentetate dimeglumine and **c** after additional gadopentetate dimeglumine to make up a total dose of 0.1 mmol/kg b.w. Differentiation between recurrent tumour and ipsilateral temporal lobe of this atypical macroadenoma extending through the left cavernous sinus to become a space-occupying lesion of the left middle cranial fossa was facilitated by the contrast-medium-enhanced images

ages were evaluated by three neuroradiologists (J.K.H., S.J.B., H.K.P.), who were blinded to each other's interpretations. Tumour extension was evaluated according to the SIPAP classification system [11]. SIPAP is an acronym for the five juxtasellar directions of pituitary tumour extension, i.e., suprasellar, infrasellar, parasellar, anterior and posterior, and is the name of an MR classification system for pituitary adenomas. The conspicuity of lesion margins was scored using an arbitrary scale of 1–5 (1 = indistinct, 5 = well defined). For statistical purposes the observers made consensus agreement on the tumor conspicuity scores in case of differing scores at the initial blinded readings. A generalized Cochran-Mantel-Haenszel (CMH) test was used to evaluate differences in these scores [12]. Signal intensity measurements were obtained from the most enhancing part of the adenoma, from the three sets of coronal images. Signal intensity measurements of the air outside the skull were obtained as an indication of background noise, and these values were subtracted from the signal intensity measurements of normal brain and adenomas prior to the calculation of percentage change in signal intensity [13].

Results

The CM-enhanced imaging sequences were completed within 20 min in all patients. Pre-, reduced- and full-CM injection images were available in all patients. For each patient the same tumour remnants were identifiable on all imaging sequences, and tumour extension according to the SIPAP classification system was the same comparing the pre- and two post-CM-injection sequences of coronal T1WI (Figs. 1, 2, 3). However, the differentiation between recurrent tumour and ipsilateral temporal lobe was improved by CM-enhanced images in 1 patient (Fig. 3).

With respect to tumour conspicuity, 54 images were scored (Table 1). Of a total of 162 scores made by three neuroradiologists, the observers disagreed on eight scores in five patients. The CMH test did not demonstrate any significant differences comparing the conspicuity scores of the reduced- and full-CM-dose groups with each other ($p = 0.564$). Excepting the somewhat unusual macroadenoma of patient 15 (Fig. 3), the full-dose images did not score better than the reduced-dose images in any one patient, whereas the opposite was true in three patients. However, the CMH tests did demonstrate significantly better conspicuity scores of the reduced-CM-dose images compared with the pre-CM-injection images ($p = 0.001$) and of the full-CM-dose images compared with the pre-CM-injection images ($p = 0.001$).

Average signal intensity measurements were available in 16 surgically treated macroadenomas prior to and following the two different doses of intravenously injected gadopentetate dimeglumine (Fig. 4). Mean percentage signal increase following the injection of 50% of a dose of 0.1 mmol/kg b.w. of gadopentetate dimeglumine was 44% (range 4–75%), and the mean percentage signal increase following the intravenous injection of 0.1 mmol/kg b.w. in 16 surgically treated macroadenomas was 77% (range 15–152%; Fig. 5).

Table 1. Ratings of conspicuity of tumour margins in 18 surgically treated macroadenomas at different doses of intravenous contrast medium. *Pre* prior to contrast medium injection; *reduced* 50% of full dose; *Full* full dose

Patient no.	Score		
	Pre	Reduced	Full
1	4	5	5
2	4	5	5
3	4	5	5
4	4	5	4
5	4	4	4
6	4	4	4
7	4	4	4
8	5	5	5
9	5	5	5
10	3	4	4
11	3	4	4
12	3	4	4
13	3	4	3
14	3	4	3
15	2	3	4
16	4	5	5
17	4	5	5
18	3	4	4
Mean	3.7	4.4	4.3
SD	0.77	0.61	0.69

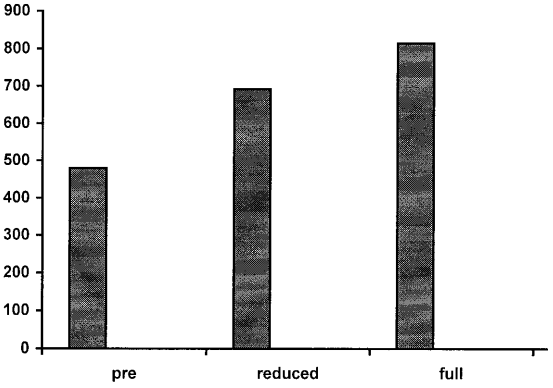

Fig. 4. Average signal intensity measurements (*y*-axis) in 16 surgically treated macroadenomas; prior to contrast medium injection *(pre)*, following reduced contrast medium dose administration *(reduced)* and following full contrast medium dose administration *(full)*

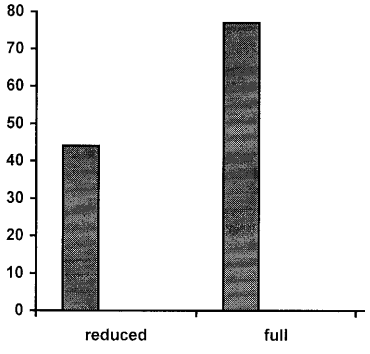

Fig. 5. Mean percentage signal increase (*y*-axis) in 16 surgically treated macroadenomas after intravenous contrast medium injection of 50% *(reduced)* or 100% *(full)* of the commonly recommended dose of 0.1 mmol/kg b.w. of gadopentetate dimeglumine

Discussion

Magnetic resonance imaging of macroadenomas should result in accurate definition of tumour location, demarcation relative to surrounding structures and differentiation between different tumour components, because medical therapy, surgical approach and stereotactic procedures, such as gamma knife treatment, radiation therapy or tumour observation may all be altered by these variables. Previous reports have indicated that macroadenomas may be well visualized on unenhanced T1-weighted MR images [5, 14, 15], but it has also been suggested that the use of CM-enhanced T1WI in the preoperative evaluation of these tumours may be justified [14].

In the present study of surgically treated macroadenomas the CM-enhanced MR images gave additional diagnostic information in 1 patient only. The differentiation between recurrent adenoma extending into the middle cranial fossa, and the ipsilateral temporal lobe of patient 15, was clearly facilitated by the CM-enhanced MR images. Although the full-CM-dose images of this 1 patient scored better than the reduced-dose images, the reduced-CM-dose images should suffice.

Visual assessment by observers more than numerical signal intensity values is of importance in the accurate diagnosis of radiological findings. Except for patient 15, the apparently improved tumour conspicuity comparing CM-enhanced with unenhanced MR images did not result in any additional pathological findings and no changes in diagnosis between the groups were made.

Macroadenomas may reach, indent or infiltrate the cavernous sinuses. The marked hyperintensity of the cavernous sinuses following the injection of 0.1 mmol/kg Gd-DTPA, adjacent to a contrast-enhancing macroadenoma, does not always facilitate the accurate demarcation between these two structures. It has been suggested that this dose of CM results in such a marked hyperintensity of the pituitary gland and surrounding structures including the cavernous sinuses that the enhancement may be detrimental to the detection of small pituitary lesions, and accurate definition of the medial cavernous sinus [2]. The present study did not demonstrate any improvement in the definition of the interface between macroadenoma and cavernous sinus comparing the unenhanced T1WI with the reduced- or with the full-CM-dose T1WI in the same patients.

In their study of contrast enhancement of brain tumours, Chang and colleagues [9] did not observe any difference in contrast enhancement between the single- and double-dose images in the majority of meningiomas and neurinomas at a given field strength. As demonstrated in Figs. 1, 2 and 3 this was not the case in the present study. Tumour enhancement did vary with different doses of contrast medium in this series of 18 surgically treated macroadenomas. The variations were so great that it was impossible to evaluate the images in a blinded fashion with respect to the given CM dose.

Contrast medium enhancement in MR imaging depends on several factors including magnetic field strength, CM dose and time interval from CM injection to imaging [9, 16, 17, 18]. It has been shown that the de-

gree of CM enhancement was significantly higher at 2.0 and 1.5 T than on 0.5 and 0.3 T, respectively [3, 9]. All the MR examinations in the present study were performed on the same 1.5-T MR machine, and completed within 20 min of the first CM injection. Cumulative dose studies, like the present study design, have previously been used both in the study of intra- and extra-axial lesions [5, 7, 10], and the validity of this study design has been confirmed [18].

Contrast-medium-enhanced MR imaging is a powerful tool in the work-up of intracranial lesions. The decision whether or not to use intravenous CM in a particular MR imaging study has important diagnostic, medicolegal and economical implications. Pituitary macroadenomas due to their location and potential for regrowth with compromise of important adjacent structures may require lifelong tumour-size monitoring with MR imaging as the preferred imaging method. In this context the decision whether to use intravenous CM at all, and at which dose, may have important economical consequences for both patients and health care providers.

Although the optimal CM dose has yet to be decided, it can be defined as that which, with no adverse effects, gives the best demonstration of normal anatomy and pathological changes. For the patient the ideal CM dose should be the lowest dose available that assures optimal treatment. To receive this ideal dose should be a " right" of the patient and an obligation for the physician to prescribe. This dose may of course be zero, but no such dose exists as the optimal dose of Gd-DTPA-based contrast media vary with several factors including magnetic field strength and type of lesion.

Accurate identification and delineation of residual or recurrent tumour following pituitary adenoma surgery is important. Our findings indicate that CM-enhanced studies are not routinely required for postoperative MR evaluation of pituitary macroadenomas. However, if a CM-enhanced MR study is deemed necessary, this may be done with a reduced dose of CM, as CM dose reduction is not detrimental to accurate identification and delineation of surgically treated pituitary macroadenomas.

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