Clin Neuroradiol (2019) 29:117–123
https://doi.org/10.1007/s00062-017-0628-2

ORIGINAL ARTICLE

Low-Dose CCT to Exclude Contraindications to Lumbar Puncture

Benefits and Limitations

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Received: 7 May 2017 / Accepted: 9 September 2017 / Published online: 30 September 2017

Abstract
Background Low-dose cranial computed tomography (LD-CCT) based on iterative reconstruction has been shown to have sufficient image quality to assess cerebrospinal fluid spaces (CSF) and midline structures but not to exclude subtle parenchymal pathologies. Patients without focal neurological deficits often undergo CCT before lumbar puncture (LP) to exclude contraindications to LP including brain herniation or increased CSF pressure. We performed LD-CCT to assess if image quality is appropriate for this indication.
Methods A total of 58 LD-CCT (220 mA/120 kV) of patients before LP were retrospectively evaluated and compared to 79 normal standard dose cranial computed tomography (SD-CCT) (350 mA/120 kV). Iterative reconstruction used for both dose levels was increased by one factor for LD-CCT. We assessed the signal-to-noise (SNR) and contrast-to-noise ratio (CNR), the dose estimates and scored diagnostic image quality by two raters independently. Significance level was set at $p < 0.05$.
Results The inner and outer CSF spaces except the sulci were equally well depicted by the LD-CCT and SD-CCT; however, depiction of the subtle density differences of the brain parenchyma and the sulci was significantly worse in the LD-CCT ($p < 0.0001$). The SNR in the gray matter (9.35 vs. 10.61, $p<0.05$) and white matter (7.23 vs. 8.15, $p<0.001$) were significantly lower in LD-CCT than in SD-CCT with significantly lower dose estimates (1.04 vs. 1.69 mSv, respectively $p<0.0001$).
Conclusion The use of LD-CCT with a dose reduction of almost 50% is sufficient to exclude contraindications to LP; however, LD-CCT cannot exclude subtle parenchymal pathologies. Therefore, in patients with suspected parenchymal pathology, SD-CCT is still the method of choice.

Keywords Computed tomography · Low dose · Iterative reconstruction · Standards · Lumbar puncture

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Introduction

Cranial computed tomography (CCT) is the second most frequent CT examination involving one third of all CTs with approximately 75% in a hospital setting [1]. The national CCT reference doses range from 2 mSv in Germany [2], 2.2 mSv in the UK [3] to 2.3 mSv in Switzerland [4], and may therefore already double the annual natural radiation dose of 2.4 mSv averaged for the entire northern hemisphere [5].

Many attempts have been made to reduce the patient CCT dose, such as automatic tube current modulation or noise reduction filters; however, those attempts failed due to an inacceptable noise increase [6, 7]. Not before 2009 the trade-off between the need of high quality low-noise CCT images and the desired use of low doses of radiation seemed to be revolutionized by the establishment of iterative reconstruction (IR) techniques. Although IR techniques were already known for the first CT scanners in the 1970s [8], they only became feasible through the technical progress with more powerful processors [9]. The IR techniques allow dose reduction by modifying raw or CT

Table 1 Dose estimates of the LD-CCT (220 mAs) and the SD-CCT (350 mAs) in comparison

	$CDTI_{vol}$ (mGy)	DLP (mGy × cm)	ED (mSv)
LD-CCT	34.6	453.16	1.04
SD-CCT	54.95	732.89	1.69
P-value	<0.00001	<0.00001	<0.00001

CCT cranial computed tomography, *LD* low dose, *SD* standard dose, $CTDI_{vol}$ weighted volume computed tomography dose index, *DLP* dose length product, *ED* effective dose

image data to reduce noise while preserving spatial resolution and the missing imaging data are replaced based on a complex calculation model [9]. It has recently been shown that radiation dose of CCT can be considerably reduced using IR techniques to monitor intracranial hemorrhage (ICH) [10–13]. However, it is known that with increasing dose reduction and increased calculated data, image information might be lost [10]. This might be a problem especially in CCT, in which subtle density differences of gray and white matter have to be assessed, for example in stroke diagnostics [10, 14]. In the daily neurological routine, exclusion of increased intracranial pressure and brain herniation as contraindications to lumbar puncture to rule out meningitis or subarachnoid hemorrhage is a frequently asked question to CCT [15–17]. Dose reduction would be particularly desirable in those patients because they are usually of younger age and do not show focal neurological signs.

Papilledema in funduscopy is a very sensitive clinical sign for increased intracranial pressure.However, the specificity of funduscopy is low including pathologies ranging from neoplasms to sinus thrombosis and pseudotumor cerebri [18].Therefore, patients with papilledema should also necessarily undergo CCT before lumbar puncture to avoid brain herniation.

Based on the promising results of previous low-dose CCT studies [10–13, 19–27], we aimed to investigate if assessment of CT morphological contraindications to lumbar puncture is sufficiently possible using dose-reduced CCT. We therefore performed a retrospective analysis of diagnostic image quality of low-dose cranial CT (LD-CCT) in younger patients indicated to rule out contraindications to lumbar puncture. Moreover, we compared diagnostic image quality of LD-CCT with standard dose cranial CT (SD-CCT) of similarly aged patients.

Patients and Methods

Study Population

The institutional ethics committee approved the retrospective CCT data analysis for this study. The requirement for patient informed consent was waived by the institutional review board. All CTs were based on clinical indications and no extra CT scans were performed for study purposes.

We retrospectively analyzed adult patients (between 18 and 50 years). We included all consecutive patients referred from our neurological emergency department, who were scheduled for lumbar puncture to exclude meningitis or subarachnoid hemorrhage, presenting with or without headaches and no focal neurological signs besides isolated peripheral facial nerve palsy. The patients received a LD-CCT between October 2013 and October 2014. All consecutive adult patients between 18–50 years referred from the neurological emergency department during the same time period presenting with focal neurological deficits and receiving a SD-CCT were also included as the control group. We excluded all CCT with relevant motion or metal artifacts.

Definition of Low-Dose and Standard Dose CCT, Image Acquisition and Reconstruction Parameters

All patients were scanned on a 64-multidetector CT scanner (Ingenuity Core, Philips Healthcare, Eindhoven, The Netherlands). With the installation of an IR-compatible CT scanner in our institution (October 2013), an IR-based SD-CCT protocol was first implemented for clinical use by a committee of experienced neuroradiologists and the manufacturer's application specialists. On this basis, a stepwise reduction in radiation dose and increase of the IR factor was performed to subjectively balance the highest possible dose reduction and sufficient image quality in LD-CCT to exclude contraindications to lumbar puncture but without claiming to deliver sufficient image quality to assess subtle density differences of the brain parenchyma. In contrast, the SD-CCT protocol was dedicated to deliver optimal image quality to evaluate even subtle density differences of the brain parenchyma.

The CT imaging parameters included axial mode with a collimation of 16 × 0.6 mm with a scan increment of 10 mm, a reconstruction slice thickness of 5 mm, and a rotation time of 1 s. We used a tube current of 350 mAs, a tube voltage of 120 kV, and an IR factor of 1 (algorithm iDose [28]) for SD-CCT with a mean weighted volume CT dose index ($CTDI_{vol}$) of 54.95 mGy which corresponds to 92% of the national reference $CTDI_{vol}$ for CCT. For LD-CCT the tube current was reduced to 220 mAs (algorithm iDose level 2) with a mean $CTDI_{vol}$ of 34.6 mGy resulting in 58%

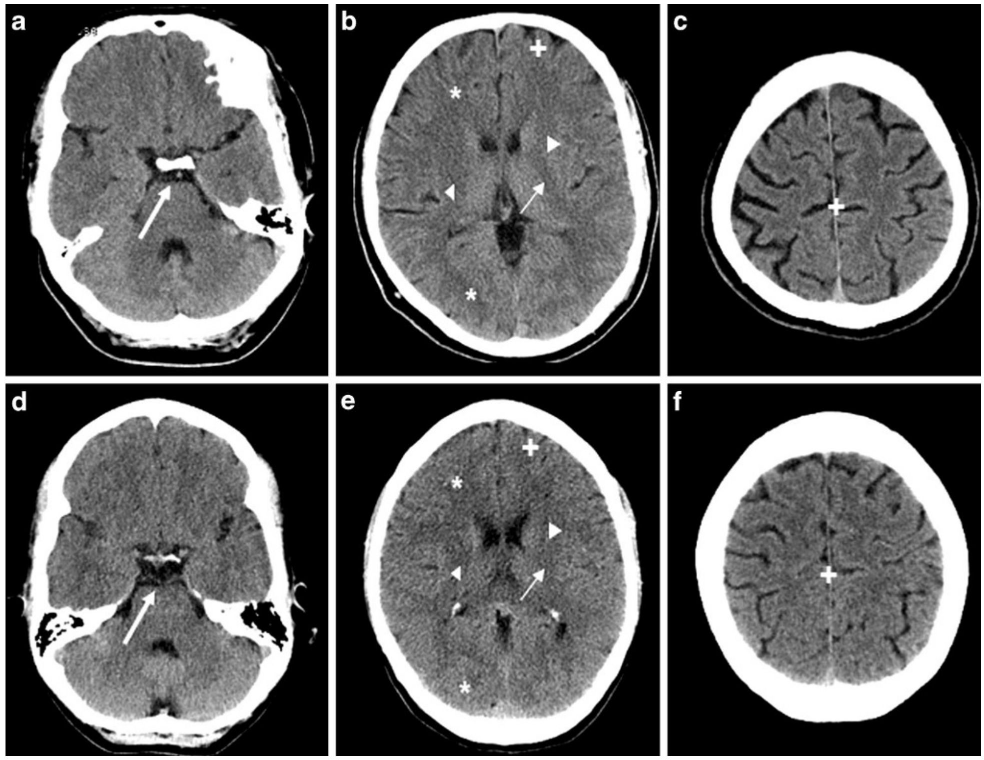

Fig. 1 (**a–c**) SD-CCT (350 mAs) in comparison to LD-CCT (220 mAs) of two patients in their third decade of life (**d–f**). Please note the better visibility of the gray matter and white matter border (*asterisk**), the insular ribbon (*arrowhead*), the basal ganglia and the internal capsule (*thin arrow*) and of the sulci (*white cross*) in the SD-CCT (350 mA), whereas the ventricles and basal cisterns (*thick arrow*) are equally well depicted in the LD-CCT (220 mAs) excluding contraindications to lumbar puncture

of the national reference $CTDI_{vol}$ [2]. All reconstructions were performed with a standard ultrahigh-resolution (UB) window kernel [29, 30].

Contrast-To-Noise (CNR), Signal-To-Noise Ratio (SNR) and Dose Estimates

We determined the contrast-to-noise ratio (CNR) and signal-to-noise ratio (SNR) as objective quantitative image analysis parameters in all patients. For signal analysis, regions of interest (ROIs) were manually drawn in the gray matter (GM) and in the white matter (WM) of the superior frontal gyrus (by S.A.). The mean attenuation values of the GM and WM-ROIs in the frontal brain were divided according to the noise level (equal to the standard deviation) to calculate the SNR [11]. The CNR was defined according to the formula: $(\text{mean GM}-\text{mean WM})/[(SD \times GM)^2 + (SD \times WM)^2]^{0.5}$ [24]. For the estimation of radiation doses, we recorded the dose length product (DLP in mGy × cm) and the $CTDI_{vol}$ (in mGy) from the patient protocol. The effective dose (ED) was calculated as a product of DLP and the conversion factor of the head (0.0023 mSv/Gy × cm) [11].

Analysis of Diagnostic Image Quality Parameters

Diagnostic image quality parameters were independently assessed by an experienced neuroradiologist (by S.B. with 7 years of neuroradiology experience) and by a medical student with 1 year of training in reading CCTs (by S.A.). The training was performed by two neuroradiologists from our department (by S.B. and M.W) and focused on how to identify and rate the anatomical structures listed in the questionnaire used for image quality analysis, the precentral and postcentral gyrus and the correct ROI placement for SNR and CNR assessment.

All CT images were visually rated on a PACS workstation (GE Centricity 2011, Ris-i4.2 plus; Boston, MA, USA). Both raters were blinded to the dose protocol, patient information (name, sex and age) and acquisition date. Image quality was defined according to a predefined questionnaire grading the conspicuousness of 1) the gray matter and white matter differentiation, 2) the ventricles, 3) the sulci, 4) the basal ganglia and internal capsule, 5) the foramen magnum, 6) the basal cisterns, 7) the insular ribbon and 8) the visual impression by a 3-point score system (1 = good, 2 = moderate, 3 = poor) [10].

Statistical Analysis

We compared visual and objective image quality (SNR, CNR) of LD-CCT and SD-CCT. All statistical analyses were performed using BIAS™ Version 10.12 software (2014 Epsilon, Frankfurt, Germany) with a significance level of $p < 0.05$. Because of non-normally distributed values DLP and $CTDI_{vol}$, SNR (WM and GM), CNR and subjective image quality rating, as well as age were statistically evaluated by the Wilcoxon-Mann-Whitney U-test.

Table 2 Comparison of subjective image quality scorings of the SD-CCT and LD-CCT by rater 1

	SD-CCT (*n* = 79)			LD-CCT (*n* = 58)			*P*-value
Category (score)	1	2	3	1	2	3	
GM/WM differentiation	71	8	0	9	48	1	<0.0001
Ventricles	79	0	0	56	2	0	0.096
Sulci	78	1	0	38	20	0	<0.0001
BG and IC	75	4	0	22	36	0	<0.0001
Foramen magnum	79	0	0	58	0	0	Ø
Basal cisterns	79	0	0	58	0	0	Ø
Insular ribbon	70	9	0	8	49	1	<0.0001
Visual impression	73	6	0	11	46	1	<0.0001

SD-CCT standard dose cranial computed tomography, *LD-CCT* low dose cranial computed tomography, *GM/WM* gray matter and white matter, *BG and IC* basal ganglia and internal capsule
Ø statistically not evaluable

Interobserver agreement of subjective image quality ratings concerning the SD-CCT and LD-CCT were assessed with Cohen's kappa test.

Results

Study Population

We included 137 consecutive adult patients (between 18–50 years) from the neurological emergency department undergoing a LD-CCT or SD-CCT into the analysis. Of the patients 58 received a LD-CCT and 79 patients a SD-CCT. The mean age ± standard deviation (SD) of the patients ($n = 79$) undergoing CCT with a standard dose was 36 ± 8 years and the mean age ± SD of the patients ($n = 58$) receiving a LD-CCT was 31 ± 12 years. The patient group receiving a LD-CCT was significantly younger ($p < 0.001$). Justifying indications for LD-CCT were exclusion of contraindications to lumbar puncture (74.1% (43/58) of patients presented with headache and/or fever and isolated peripheral facial nerve palsy with no other focal neurological signs).

After LD-CCT 53.4% (31/58) of patients underwent lumbar puncture after a thorough neurological examination, another 12.1% (7/58) of patients refused the neurologically indicated procedure. Final diagnoses at hospital discharge of the 58 LD-CCT patients were migraine or unspecific headache without signs of meningitis or subarachnoid hemorrhage (40/58, 69%), peripheral nerve lesion (5/58, 8.6%), meningitis (9/58, 15.5%), pseudotumor cerebri (2/58, 3.4%), paranoid episode (1/58, 1.7%) and hypotension headache after lumbar puncture (1/58, 1.7%). An SAH was not diagnosed in any patient by LD-CCT or by lumbar puncture. Dose estimates and SNR and CNR, DLP, $CDTI_{vol}$ and ED were significantly smaller using LD-CCT than with SD-CCT (Table 1). The SNR of WM and GM was significantly lower in the LD-CCT compared to the SD-CCT with 7.23 vs. 8.15 ($p = 0.00083$) and 9.35 vs. 10.61 ($p = 0.0047$), respectively. There were no significant differences in the CNR of the LD-CCT and SD-CCT with 1.6 vs. 1.68 ($p = 0.25$).

Diagnostic Image Quality Parameters

Overall imaging quality was sufficient in all evaluated CCTs. Furthermore, in none of the LD-CCT patients was it necessary to perform additional SD-CCT because of insufficient image quality. There were no differences in the image quality of the ventricles, the basal cisterns and the foramen magnum between the LD-CCT and SD-CCT. Both raters found the imaging quality of the gray matter and white matter differentiation, the sulci, the basal ganglia and the internal capsule, the insular ribbon and the visual impression to be significantly better in the SD-CCT than in the LD-CCT ($p < 0.0001$, Fig. 1; Table 2 and 3).

Interobserver Reliability

Visibility of the ventricles, foramen magnum and basal cisterns were rated equally in the LD-CCT and SD-CCT by both raters (Table 2 and 3). There was a good interrater agreement concerning perception of the gray matter and white matter differentiation, the insular ribbon, the foramen magnum, the basal cisterns, the ventricles and of the visual impression ($\kappa \geq 0.6$, $p < 0.0001$). Both raters accredited SD-CCT to deliver better imaging quality of the basal ganglia and internal capsule, as well as the sulci. The interrater agreement for the conspicuousness of the basal ganglia and internal capsule was moderate in both the LD-CCT and SD-CCT (each $\kappa = 0.5$, $p < 0.001$). There was a moderate agreement concerning the imaging quality of the sulci in SD-CCT ($\kappa = 0.5$, $p < 0.0001$) and a good in-

Table 3 Comparison of subjective image quality scorings of the SD-CCT and LD-CCT by rater 2

	SD-CCT (n = 79)			LD-CCT (n = 58)			P-value
Category (score)	1	2	3	1	2	3	
GM/WM differentiation	71	8	0	9	48	1	<0.0001
Ventricles	79	0	0	56	2	0	0.096
Sulci	76	3	0	36	22	0	<0.0001
BG and IC	69	10	0	22	36	0	<0.0001
Foramen magnum	79	0	0	58	0	0	Ø
Basal cisterns	79	0	0	58	0	0	Ø
Insular ribbon	72	7	0	6	50	2	<0.0001
Visual impression	72	7	0	11	44	3	<0.0001

SD-CCT standard dose cranial computed tomography, *LD-CCT* low dose cranial computed tomography, *GM/WM* gray matter and white matter, *BG and IC* basal ganglia and internal capsule
Ø statistically not evaluable

terrater agreement for the sulci assessment in LD-CCT (κ = 0.8, $p < 0.0001$).

Discussion

The results of the current study revealed that contraindications to lumbar puncture in neurological patients, such as signs of increased intracranial pressure and brain herniation [15–17], can be excluded by LD-CCT with dose reduction to almost half of the reference value. Previous studies on LD-CCT already showed promising results in comparison to SD-CCT regarding analysis of diverse quantitative and qualitative image parameters [10–13, 19, 20, 22–27].

We created an LD-CCT protocol delivering only 57.7% of the national reference $CTDI_{vol}$ on average and 53.3% of the reference DLP using IR techniques [2]. Compared to the filtered back projection technique, IR techniques modify raw and CT image data to separate image information and image noise. Iterative processing loops are applied to the data to reduce noise while preserving spatial resolution, and the missing image data are replaced based on a complex calculation model [9]. However, IR algorithms do not primarily reduce the absorbed radiation dose in CT scanning but use iterative steps of noise reduction to maintain a sufficient level of image quality at reduced dose levels [9]. Therefore, with increasing IR factor and dose reduction, as applied in our LD-CCT protocol, more image data have to be replaced by calculation, potentially leading to a loss of image information, especially concerning subtle density differences [10]. Correspondingly, structures with higher density differences to the surrounding structures including cerebrospinal fluid (CSF) spaces (ventricles and basal cisterns) were equally well assessable in the LD-CCT and SD-CCT, whereas structures with subtle density differences including gray and white matter junction, basal ganglia, internal capsule, and the insular ribbon were significantly worse distinguishable using LD-CCT. However, those structures are all highly relevant for CT assessment of patients with focal neurological deficits especially including stroke diagnostics [14, 31]. Bodelle et al. [25] proposed no relevant loss of image information to assess acute ischemic lesions by IR-based LD-CCT with a dose reduction of 23% in comparison to their SD-CCT protocol. However, the authors reported inclusion of ischemic lesions evident on CT due to ethical reasons, since patients with more acute events underwent magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI). Therefore, early CCT signs of cerebral infarctions [14, 31] might not have been evaluated.

While it has recently been shown that the radiation dose of CCT can be considerably reduced using IR techniques to monitor ICH [10–13], it could be argued that LD-CCT is sufficient to exclude hemorrhage in acute stroke patients prior to i. v. thrombolysis. However, CT evaluation of early signs of infarction play a significant role in endovascular stroke treatment, especially for excluding patients from endovascular stroke treatment in case of extended ischemic core [32]. Our results regarding the impaired assessability of parenchymal brain structures using LD-CCT are in line with the literature, where an inferior conspicuousness of the gray and white matter border [10, 12], basal ganglia [13] and of edematous lesions [10] were described.

In contrast to ventricles and basal cisterns, the outer CSF spaces along the brain surface could be assessed significantly better on SD-CCT compared to LD-CCT. This contrasts with the results of previous studies [10, 20] and might be explained by the younger age of our patient collective (all patients were ≤50 years of age with mean ages of 36 and 31 years for the SD-CCT and LD-CCT patients, respectively) and their correspondingly larger brain volume leading to smaller density differences because of smaller amounts of hypodense CSF in the sulci. Furthermore, stronger beam hardening artifacts could have contributed to their poorer assessability on LD-CCT in our study. As a consequence, in patients with a suspected pathology of the sulci along the brain surface, i. e. SAH, we strongly recommend that SD-CCT should be performed. In fact, SAH might even be missed by SD-CCT requiring additional lumbar punctures to exclude SAH [33–35]. However, focal SAH or subpial hemorrhage (for instance due to cerebral amyloid angiopathy or venous thrombosis) might also be missed by CSF analysis. Therefore, additional MRI might be necessary in patients with discrepancies between clinical symptoms and unremarkable CCT and lumbar puncture. In the current study, SAH was not diagnosed in any patient either by LD-CCT or by lumbar puncture.

As expected and previously described [19, 20, 24, 27] SNR was significantly lower in LD-CCT than in SD-CCT, claiming that LD-CCT has inherent objective image quality deficits. However, CNR did not differ between the two CT protocols. Moreover, it has been questioned whether quantitative measurements are appropriate for evaluating the effectiveness of IR algorithms.

Our Study has Several Limitations First, no explicit patient group matching was performed. We included adult patients of 50 years of age or younger, since these patients would especially profit from CCT dose reduction [36]. Although we used defined inclusion criteria for LD-CCT and SD-CCT and retrospectively analyzed all consecutive adult patients meeting these criteria in a fixed period (from October 2013 to October 2014), the fact that the group of patients receiving LD-CCT were significantly younger might be due to a selection bias for choosing LD-CCT in younger patients more often.

Second, comparison of the diagnostic image quality parameters of the low dose and SD-CCT were based on the subjective impression of two raters; however, an experienced reader may primarily identify a LD-CCT by its typical appearance subconsciously influencing the analysis. Therefore, we also performed objective quantitative image analysis to validate qualitative evaluation. Further, there are no general guidelines for the distinct assessment and evaluation of LD-CCT in the first place.

Third, the sample size of our retrospective study was quite low.

Fourth, use of thin source images and their multiplanar reconstruction may increase diagnostic sensitivity for small pathologies, such as focal SAH compared to the thicker reconstructed images, although beamhardening artifacts may also increase.

Fifth, we did not perform a distinctive phantom-based image quality analysis of the various steps of dose reduction and iterative strength.

Finally, results of LD-CCT studies should be compared with caution. Although our results are in line with the literature in most parts, the comparability between studies from different institutions and different CT scanners is restricted. Up to now, there is neither consent as to which parameters actually characterize the diagnostic value of LD-CCT, nor are there any general technical instructions on how LD-CCT should be acquired or reconstructed. Our SD-CCT and LD-CCT protocols are institutional and scanner-specific, and may not be feasible in other settings. The IR algorithms and therefore noise properties vary for each CT scanner and manufacturer [9] and their strength levels may be individually chosen. Consequently, image quality parameters, such as gray matter and white matter differentiation and visual impression in LD-CCT with IR might not only rely on the dose reduction and the corresponding noise increase, but may also be dependent on the applied IR algorithm and level, as well as the extent of noise decrease and data replacement.

Further large multicenter investigations with different CT scanners and manufacturers are needed to learn more about the effects of iterative strength levels and algorithms on image quality parameters besides the effects of dose reduction. Finally, guidelines for LD-CCT application in clinical practice with uniform parameters of image acquisition/ reconstruction and image quality assessment need to be established.

Conclusion

The use of LD-CCT with approximately one half of the current national radiation reference dose is feasible to exclude contraindications to lumbar puncture.

Acknowledgements We declare no financial conflict of interests. The work was part of a scientific cooperation between our institute and Philips Healthcare (Hamburg, Germany). The authors state that this work has not received any funding by the company. We received constant technical support from Philips Healthcare.

Conflict of interest S. Blasel, S. Alex, H. Ackermann, J. Tichy, J. Berkefeld and M. Wagner declare that they have no competing interests.

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