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T1 Gd-enhanced compared with CISS sequences in retinoblastoma: superiority of T1 sequences in evaluation of tumour extension

Received: 24 February 2004
Accepted: 3 November 2004
Published online: 14 January 2005
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Abstract *Background:* As adequate therapy for retinoblastoma in young children depends on infiltration of extra-retinal structures, diagnostic modalities play an essential role. *Methods:* In this widely extended study, 80 children with retinoblastoma were studied with MRI (standard fat-suppressed Gd-enhanced T1, T2 thin-slice sequences (additionally with small loop surface coil), constructive interference in steady state (CISS) sequence covering the orbita). The images were analysed by two blinded neuroradiologists. Histology was used as the gold standard. *Results:* MRI assumed infiltration of extra-retinal structures in 13 of 80 patients of which ten were confirmed by histology. Affected extra-retinal structures were: optic nerve (five, of which two were on CISS and three on T1 with higher image resolution using the surface coil), scleral infiltration (five, of which four on CISS and T1) and

ciliary body infiltration (one on CISS and T1). Another 61 enucleated patients did not have any extra-retinal infiltration in histology. The CISS sequence with multiplanar reconstruction was mainly helpful in revealing exact three-dimensional tumour extension with excellent clinical acceptance and pre-surgical planning but T1 fat-suppressed Gd-enhanced images were superior in revealing exact tumour extension. *Conclusion:* CISS sequences allow to produce excellent anatomical images and to perform multiplanar reconstruction to better demonstrate tumour extension. However, T1-weighted sequences after contrast application are more sensitive (60 versus 40%) in detecting infiltration of the optic nerve but equal in detecting scleral infiltration.

Keywords retinoblastoma · ophthalmology · pediatrics · magnetic resonance

Introduction

Retinoblastomas are common retinal tumours in newborn and young children [1]. The incidence of retinoblastoma is given with 1.9/100,000: about 40% are bilateral, mostly hereditary, manifestations [1]. The classification of retinoblastomas is oriented on the prognosis and treatment modalities.

Treatment of retinoblastoma depends on laterality, intraocular tumour location, and degree of tumour extension [2, 3]. Apart from external beam radiother-

apy, new therapy concepts using polychemotherapy with additional local treatment with hyperthermia, brachytherapy, and cryocoagulation have been introduced [4–10]. Therefore, for adequate therapy precise diagnostic modalities are essential. The infiltration of extra-retinal structures and the exact extension of the tumour plays a key role in pre-surgical planning. CT and contrast-enhanced MR imaging are used not only to confirm the diagnosis, but to determine the extent of the intraocular tumour, document intralesional calcification, and delineate orbital or intracranial

Table 1 Histological and MR diagnosis of the retinoblastomas for each single case of optic nerve, scleral, or ciliary body infiltration. “-” indicates no infiltration, “+” indicates infiltration, “*” indicates cases in which small surface loop was used. For MR diagnosis, the first icon means CISS, the second T1-weighted images. *NR* neuroradiologist, *H* histology

Case	Optic nerve infiltration			Choroidal infiltration			Ciliary body infiltration		
	H	NR1	NR2	H	NR1	NR2	H	NR1	NR2
1	+	-/-	-/+	-	-/-	-/-	-	-/-	-/-
2	-	-/-	-/-	+	-/+	-/+	-	-/-	-/-
3*	+	-/+	-/-	+	+/+	+/+	-	-/-	-/-
4	-	-/-	-/-	+	-/-	-/-	-	-/-	-/-
5*	+	-/+	-/+	-	-/-	-/-	-	-/-	-/-
6*	+	-/+	+/+	-	-/-	-/-	-	-/-	-/-
7	+	-/-	-/-	-	-/-	-/-	-	-/-	-/-
8	-	-/-	+/+	+	+/+	+/+	-	-/-	-/-
9	-	-/-	-/-	-	-/-	-/-	+	+/+	+/+
10	-	-/-	-/-	+	+/+	+/+	-	-/-	-/-
11*	-	-/-	+/-	-	-/-	-/-	-	-/-	-/-
12	-	-/-	-/-	-	+/+	+/+	-	-/-	-/-

involvement [11]. Furthermore, these imaging techniques should aid the clinician in differentiating retinoblastoma from lesions that can simulate this tumour [12].

Constructive interference of steady state (CISS) in MR imaging is widely used for imaging the inner ear and inner auditory canal structures up to virtual endoscopy of the labyrinth [13, 14]. Furthermore, CISS sequences are additionally used for visualization of cranial nerves [15]. Yousry et al. [15] showed that most of the cranial nerves can be reliably assessed when using the 3D CISS technique. Due to its high T2-weighting and the 3D capability, we studied whether CISS could improve the diagnostic work-up in patients with retinoblastoma.

Materials and methods

Subjects

A total of 80 children, 47 male and 33 female (mean age 21 months, ranging from 4 to 68 months) with first

Table 2 Histological and MR diagnosis of infiltrative retinoblastomas. Histological and MR diagnosis of the retinoblastomas with respect to optic nerve, scleral, or ciliary body infiltration. Constructive interference in steady state (CISS) and T1-weighted contrast-enhanced images are analysed separately. The first number gives the MR diagnosis and the second number the histologic results. Sensitivity and specificity are given in brackets

	Positive histology		Negative histology	
	Optic nerve infiltration	Scleral infiltration	Optic nerve infiltration	Scleral infiltration
Neuroradiologist 1				
CISS	0/5 (0%)	5/6 (83/98%)	0	1
T1	3/5 (60/100%)	5/6 (83/98%)	0	1
Neuroradiologist 2				
CISS	2/5 (40/98%)	5/6 (83/98%)	1	1
T1	4/5 (80/100%)	5/6 (83/98%)	0	1

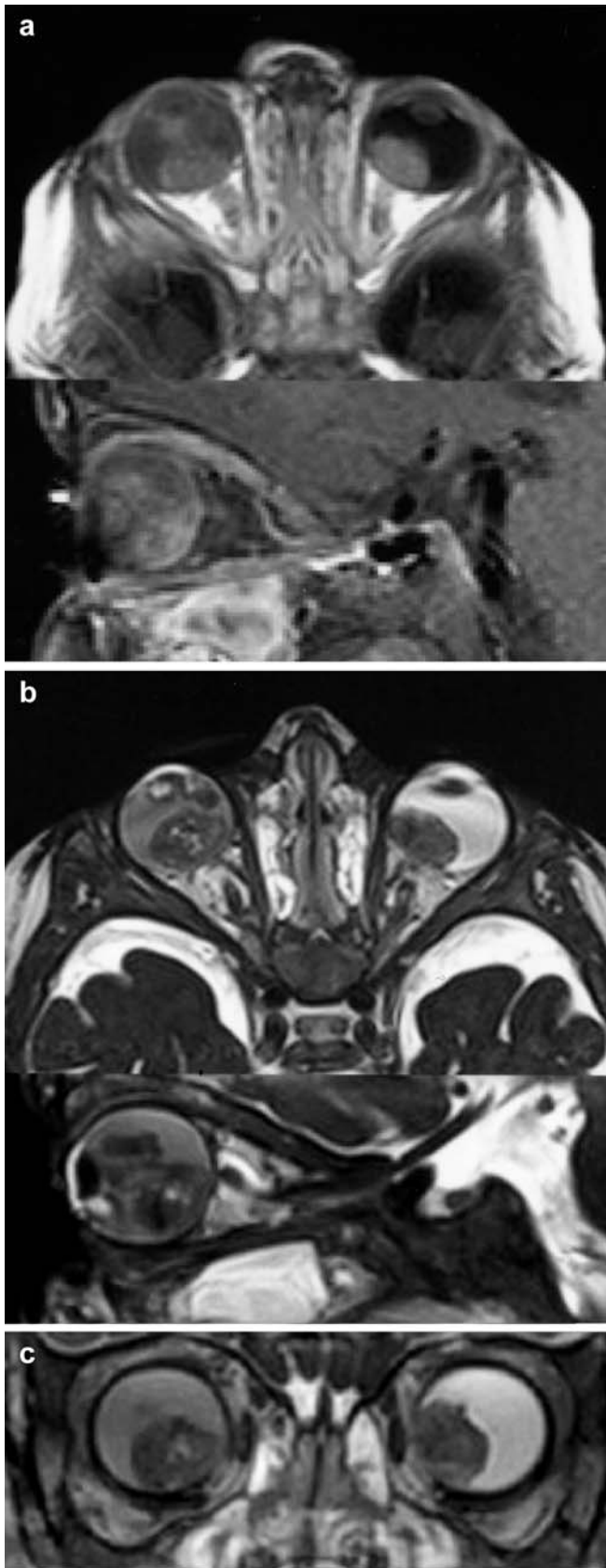
diagnosis of retinoblastoma were studied with MRI from 2000 to 2002. Histology was performed in 73 of the 80 patients, seven were not enucleated. All patients were scanned under general anaesthesia. Informed written consent for the examination was obtained from the parents.

Imaging

All MR images were acquired using a 1.5 T MR (Symphony or Sonata, Siemens, Erlangen). Imaging was performed using a standard headcoil. CISS sequence was applied with TE of 5.38 ms, TR of 10.76 ms, flip angle of 70°, field of view (FOV) of 200 mm, matrix of 256 mm and 64 slices within one slab with a resulting slice thickness of 0.6 mm. Standard transversal T1 and T2-weighted images as well as T1-weighted images with fat saturation after application of contrast agent were obtained with a slice thickness of 2 mm covering the whole orbit. The fat saturated T1-weighted had a TE 17, TR 412, flip angle 90%, FOV of 200 mm, matrix of 256 mm and 15 slices with 2 mm thickness and 0.1 mm gap. A standard dose contrast agent (Magnevist; Schering AG, Berlin, Germany) at 0.1 mmol/kg body weight was administered intravenously. Additionally, in 20 of the 80 patients transversal contrast-enhanced T1-weighted fat saturated images with a slice thickness of 2 mm and an FOV of 160 mm were obtained using a small loop coil (diameter 6 cm) fixed over the affected orbit. All transversal and sagittal slices were orientated on the course of the optic nerve. Coronal slices were not angulated and covered the whole orbit.

Analysis

All images were analysed by two blinded neuroradiologists (E.G., I.W.) with regard to image quality, spatial resolution, and tumour infiltration. Histology was used



◀
Fig. 1 A 25-month-old boy with retinoblastoma infiltration of ciliary body on the right eye. **a** High-resolution T1-weighted fat sat sequences after Gadolinium application in transversal and parasagittal slices. **b** Transversal and parasagittal reconstructed CISS images. **c** Coronal reconstructions of CISS images

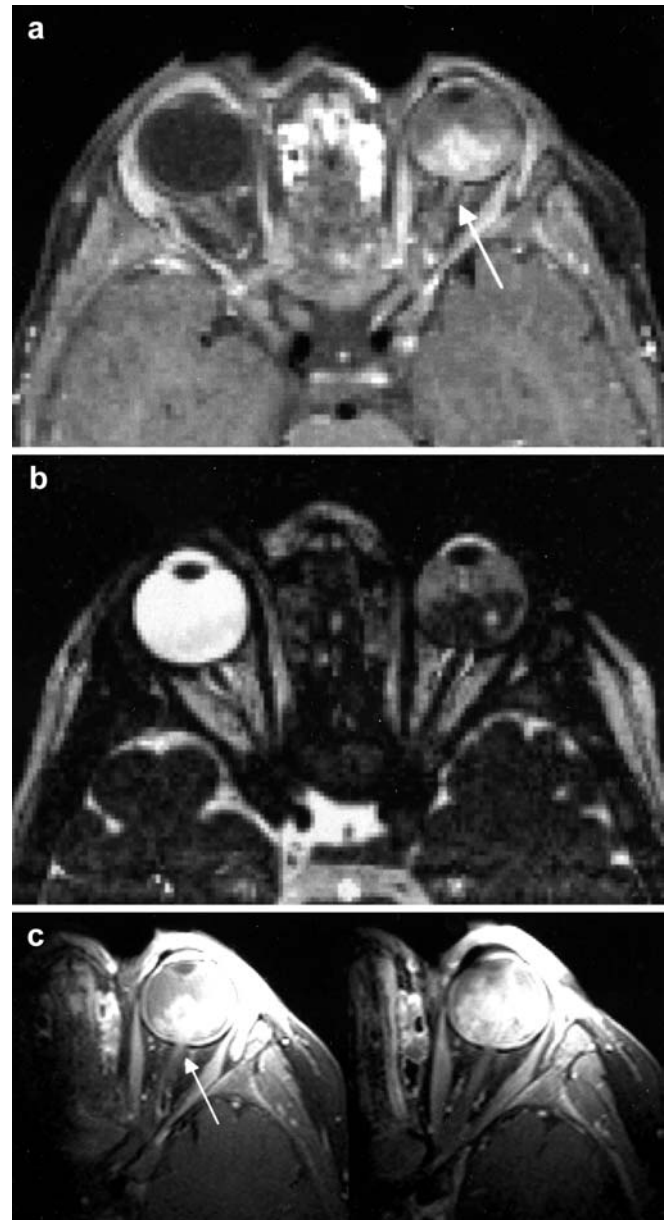


Fig. 2 A 21-month-old boy with retinoblastoma infiltration of the optic nerve on the left eye. **a** High-resolution T1-weighted fat sat sequences after Gadolinium application in transversal and parasagittal slices. **b** Transversal reconstructed CISS images did not reveal optic nerve infiltration in this case. **c** High-resolution contrast-enhanced T1-weighted transversal images with fat sat using the surface coil placed over the left eye with higher image resolution



Fig. 3 A 10-month-old girl with unilateral retinoblastoma on the left eye with extrabulbar extension. **a** Transversal reconstructed CISS images. **b** High-resolution T1-weighted fat sat sequences after gadolinium application in transversal slices

as gold standard. Sensitivity and specificity were assessed.

Clinical relevance was judged by an ophthalmologist.

Results

MRI revealed a tumour infiltration of extra-retinal structures in 13 out of 80 patients on high-resolution contrast-enhanced T1-weighted images with fat saturation or 3D CISS sequence. In ten patients, these findings were confirmed by histology revealing five optic nerve infiltration, five scleral infiltration, and one ciliary body infiltration. Two were histological negative and one was not enucleated. Of the remaining 67 patients, 61 were enucleated and did not have any optic nerve, scleral, or ciliary body infiltration in histology.

On CISS sequence all cases with optic nerve infiltration were missed by one neuroradiologist and three by the other neuroradiologist, but detection of scleral or ciliary body infiltration was possible in five of six cases by both neuroradiologists. High-resolution post-

contrast T1-weighted sequence of the orbita was superior to CISS in detecting tumour infiltration: one neuroradiologist found three of five optical nerve and five of six other tumour infiltration, the second revealed four of five optical nerve and five of six other tumour infiltrations. Table 1 shows the results of the single cases. Table 2 summarizes the histological and MRI diagnosis in respect of optic nerve, scleral, and ciliary body infiltration with sensitivities and specificities.

Figure 1 gives an example of ciliary body infiltration on the right eye, which was revealed on contrast-enhanced T1 (a) and CISS (b) images. In contrast, Fig. 2 shows an optic nerve infiltration, which was only revealed on post-contrast T1 (a) but not on CISS (b) images. Images using the surface coil led to a higher image resolution and therefore better diagnosis of optical involvement (Fig. 2c). Figure 3 gives an example of extrabulbar tumour extension in unilateral retinoblastoma on the left eye with superior depiction using Gd-enhanced T1 fat-suppressed sequence (Fig. 3b) compared to CISS (Fig. 3a).

A 53-month-old boy presented with unilateral retinoblastoma on the left eye. Figure 4 shows a comparison of head coil, small loop coil, and CISS sequence illustrating higher resolution using T1 contrast-enhanced sequences (a) compared to CISS (b) and a further improvement of resolution using the small loop surface coil (c).

High-resolution sequences using a small loop surface coil were used in 20 patients. Both neuroradiologists judged a higher image resolution in 18 patients (90%). Two patients had a poor image quality due to motion artefacts of the eye.

CISS was mainly helpful to determine the exact three-dimensional tumour extension within the eye bulb. Three-dimensional reconstruction was found to be particularly helpful as a pre-surgical tool for the ophthalmologist (Fig. 1b, c). In all 61 further cases intrabulbar tumour could be detected with T1-weighted contrast-enhanced as well as with CISS images.

Discussion

CISS sequences can optimize MR visualization of inner ear structures and cranial nerves [13, 15, 16]. Due to its high T2-weighted, this sequence reveals a high contrast between solid structures and cerebrospinal fluid in which the cranial nerves are interposed. The 3D acquisition technique allows image reconstruction in different planes and therefore excellent anatomical orientation. Especially for inner ear structures, maximum intensity projection (MIP) reconstructions are helpful to get a stereo 3D impression or perform virtual endoscopy of the labyrinth [14].

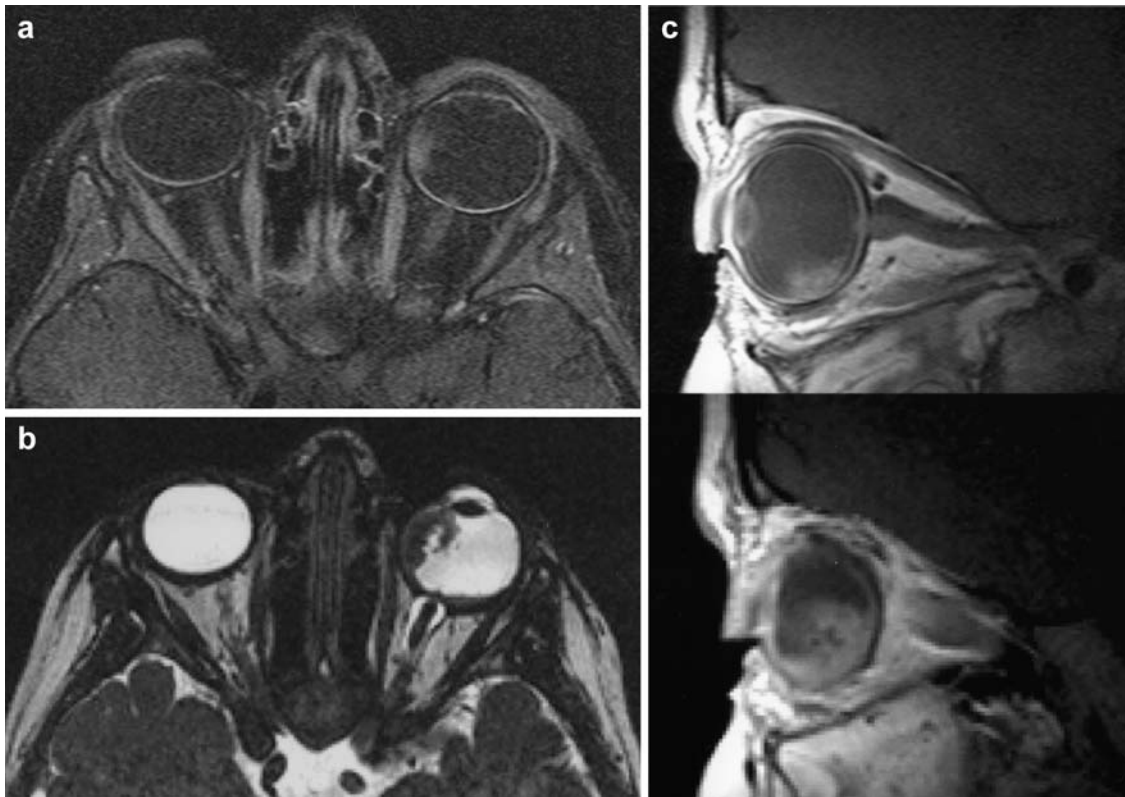


Fig. 4 A 53-month-old boy with unilateral retinoblastoma of the left eye: comparison of head coil, small loop coil and CISS sequence. **a** Transversal high-resolution T1-weighted fat sat sequences after gadolinium application using a standard head coil. **b** Transversal reconstructed CISS images. **c** High-resolution T1-weighted fat sat sequences after gadolinium application with parasagittal slice orientation using a small loop coil

The vitreous of the eye bulb is mainly of liquid consistency and tumours such as retinoblastomas represent a solid structure with mainly low signal on T2-weighted images. Therefore, we assumed that CISS sequence with its heavy T2-weighting could be a helpful tool for detection of bulbar tumours like retinoblastomas. Furthermore, a recent study has revealed increased image resolution and therefore better diagnosis [17]. Our results indicate that CISS sequences are a reliable tool in diagnostic work-up of retinoblastoma with regard to exact extension of the intrabulbar tumour but not in detecting optic nerve infiltration. In particular, the possibility of 3D image reconstructions was judged to be helpful for pre-surgical planning. However, surgical treatment normally consists of enucleation and not of partial eye bulb resection. Therefore, the most important fact is whether there is any extra-retinal infiltration because this would change clinical treatment and patients outcome [18]. The therapy in our group of patients was based on the new standards [4, 6, 7, 9, 19, 20]. Bilateral retinoblastomas were treated with polychemotherapy

and additional local therapy such as cryocoagulation or laser hyperthermia in small tumour manifestations. Large tumour manifestation were treated with polychemotherapy and additional enucleation. In all cases, individual therapeutic concepts were created to result in low recurrent rate and best possible functional results.

However, CISS images, with their good quality, do not guarantee better diagnosis with regard to judgement of infiltration of extra-retinal structures, especially optic nerve infiltration. In line with former studies, we found that post-contrast fat-suppressed T1-weighted sequences are superior to CISS in visualization of optic nerve infiltration and are therefore necessary for state of the art work-up in retinoblastomas, but even this sequence has its limitations as only cellular histological infiltration in the lamina cribrosa could not be detected with any MR sequence up to now [21]. McCaffery et al. [17] revealed better diagnosis with 3D T2-weighted images but did not analyse the extent of tumour infiltration.

As the infiltrations were histologically analysed for optic nerve, scleral, and ciliary body infiltration, we used these categories in image interpretation. We showed a difference in diagnostic reliability: our results show that optic nerve infiltration of retinoblastomas is the crucial problem on CISS sequences whereas scleral and ciliary body infiltrations could be revealed as good as with post-contrast T1-weighted images (see Table 2). One problem of this study is that we have a great number of

analysed patients with regard to image quality but only ten patients with histological infiltrations of the optic nerve, ciliary body, or sclera. Therefore, the sensitivities and specificities cannot be extrapolated for a larger group and the use of percentages has to be interpreted carefully. But CISS could be applied instead of standard T2-weighted images, which are not acquired without a gap between the single slices. High-resolution T2-weighted images are normally performed with a thickness of 2 mm and a gap of 0.2 mm and a long acquisition time for slices in one orientation [3]. CISS sequence has the opportunity of multiplanar reconstructions after acquisition in one orientation and a shorter scan time.

Phased-array surface coils allow rapid, thin-section imaging of the entire anterior optic pathway, with improved signal-to-noise ratio [22]. High-resolution sequences using a small loop surface coil in this study led to further improvement of extra-retinal and even optic nerve infiltration. However, as Schueler et al. have

shown, there is limited value in visualization of pre- and post-laminar optic nerve infiltration [3]. Analyzing image quality in 20 patients with small loop imaging gave a better image resolution in 90%. Two patients with decreased image quality with this modality were due to motion artefacts. Surface coil imaging motion is indeed a limiting factor as due to the small FOV, even little motion leads to relevant artefacts. This is also true if, like ours, the patients are under general anaesthesia. To overcome this problem it might be necessary to perform an additional retrobulbar anaesthesia.

In conclusion, CISS sequences are a reliable tool for diagnostic work-up of retinoblastoma with regard to intrabulbar extension of the tumour. However, detection of infiltration of extra-retinal structures specifically of the optic nerve post-contrast T1-weighted images are mandatory. High-resolution sequences using a small loop surface coil lead to further improvement in resolution of orbital structures.

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