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■ ONCOLOGY

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RECOMMENDATIONS FOR FOLLOW-UP

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Aims
The purpose of this retrospective study was to differentiate between the MRI features of normal post-operative change and those of residual or recurrent disease after intralesional treatment of an atypical cartilage tumour (ACT)/grade I chondrosarcoma.

Patients and Methods
We reviewed the case notes, radiology and histology of 75 patients, who had been treated for an ACT/grade I chondrosarcoma by curettage, phenolisation and bone allografting between 1994 and 2005. The first post-operative Gd-enhanced MRI scan was carried out within one year of surgery. Patients had a minimum of two scans and a mean follow-up of 72 months (13 to 169). Further surgery was undertaken in cases of suspected recurrence.

Results
In 14 patients (18.6%) a second procedure was undertaken after a mean period of 59 months (8 to 114). Radio frequency ablation (RFA) was used in lesions of < 10 mm and curettage, phenolisation and bone grafting for those ≥ 10 mm. Only six of these (8% of total) had a histologically-proven recurrence. No increase in tumour grade was seen at time of recurrence.

Conclusion
Based on this study, we have been able to classify the post-operative MRI appearances into four groups. These groups differ in follow-up, and have a different risk of recurrence of the lesion. Follow-up and treatment vary for the patients in each group. We present a flow diagram for the appropriate and safe follow-up for this specific group of patients.

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Primary central chondrosarcoma constitutes approximately 20% of malignant bone tumours, and is the third most common primary malignant bone tumour after myeloma and osteosarcoma.[1] The tumour can develop in any bone formed by enchondral ossification: most are incidental findings. The pelvis, femur and humerus are most frequently affected, whereas the small bones of the hands and feet are rarely involved (1% of all chondrosarcomas).[1-3]

Patients with an atypical cartilaginous tumour (ACT)/grade I central chondrosarcoma of a long bone have traditionally been treated by wide resection and reconstruction. This type of surgery gives good local control of the disease but often results in impaired limb function due to the sacrifice of a significant segment of bone or joint. Currently, the preferred treatment is intralesional curettage combined with at least one adjuvant treatment (cryosurgery, phenol or polymethylmethacrylate (PMMA)). Allograft can be used in preference to PMMA. Curettage is less invasive than wide resection and this technique is associated with fewer post-operative complications. It has a reported local recurrence rate of 7.5%.[4-6] The application of phenol after curettage has been shown to be beneficial in achieving tumour control *in vitro* as well as *in vivo*.[7,8]

The sensitivity of static contrast-enhanced MRI in diagnosis is well established.[9] However, the sensitivity for grading is better with dynamic contrast-enhanced imaging. This is the currently recommended method of choice and was used in this study.[10-12] The principal radiological challenge is to differentiate normal post-operative changes from those of local recurrence in the area of the bone graft. How-

Table I. Overview of imaging follow-up protocol

Time, post-operative	Patient history and physical examination	Conventional radiography	MR imaging
Before discharge		+	
6 wks		+	
12 wks		+	
6 to 12 mths*			+
2 yrs†	+		+

* introduced since 2003 as baseline MRI
† after 2 years, follow-up continues annually or every two years

Table II. Patient characteristics

Patient	Gender and age at first surgery	Group	Location of the ACT	Volume of primary tumour (cm^3)	Mths till second intervention	Type of intervention	Histology	Recurrence after second surgery	Disease-free period after second intervention (mths)
1	F, 28 yrs	II	Femur, diafysis	28	40	Curettage	Negative	No	190
2	F, 61 yrs	II	Femur, distal	1 1.9	114	TKA	NC	No	30
3	F, 38 yrs	III	Humerus, proximal	23.5	79	Curettage	Positive	No	211
4	M, 51 yrs	III	Femur, distal	36.2	90	RFA	NBT	No	65
5	F, 53 yrs	III	Humerus, proximal	5.7	8	Curettage	Negative	No	258
6	F, 16 yrs	III	Femur, proximal	45.7	25	Curettage	Positive	No	150
7	F, 41 yrs	III	Humerus, proximal	5	107	RFA	NBT	No	45
8	F, 64 yrs	III	Humerus, proximal	5.7	64	RFA	Negative	No	Unknown
9	M, 49 yrs	III	Humerus, proximal	16	32	Curettage	Negative	No	255
10	F, 39 yrs	III	Femur	48	20	RFA	Positive	No	182
11	F, 33 yrs	IV	Humerus, proximal	8.1	75	Curettage	Positive	Yes	*
12	F, 53 yrs	IV	Humerus, proximal	48.1	68	RFA	Negative	No	215
13	F, 53 yrs	IV	Humerus, proximal	52	34	Curettage	Positive	Yes	†
14	F, 56 yrs	IV	Tibia, proximal	Unknown	69	Curettage	Positive	No	116

* new small lesion on Gd-MRI two years after curettage. New RFA performed 3.5 years later
† one year and three years after RFA new lesions, re-curettage and RFA. Histology suspected for new ACT
ACT, atypical cartilage tumour; TKA, total knee arthroplasty; RFA, radiofrequency ablation; NC, non-conclusive; NBT, no biopsy taken

ever, there is limited knowledge of the post-operative findings in patients who have undergone intralesional curettage of an ACT/grade I chondrosarcoma. The published data are hard to interpret because of small patient series and different case mixes, specifically differences in location, tumour grade and the type of adjuvant used. In addition, the optimal frequency and timing of imaging after surgery are as yet unknown.

The purpose of this retrospective study was to differentiate between the MRI features of normal post-operative change and those of residual or recurrent disease after intralesional treatment of an ACT/ grade I chondrosarcoma. From this we were able to formulate a flowchart which gives the different treatment options for a suspicious lesion identified on MRI after primary treatment for an ACT/grade I chondrosarcoma.

Materials and Methods

Study population. Between 1994 and 2005, 75 consecutive patients with a histologically-proven ACT/grade I central chondrosarcoma of long bone were treated at the Leiden University Medical Center.[6] Their diagnosis was established by biopsy (34 one-stage (45%), 41 two-stage (55%)). The histological criteria were those of the 2013 World Health Oganisation classification: all histological diagnoses were reviewed.[1,13] The patient's diagnostic investigations were carried out in accordance with the European Society for Medical Oncology guidelines.[14] A gadolinium-enhanced MRI scan was undertaken preoperatively.

All patients underwent intralesional curettage followed by the application of phenol 85%/ethanol 96% to destroy any tumour cells which remained. Subsequently, the cavity left in the bone was filled with bone chips obtained from donor femoral heads (Dutch Bone Bank Foundation, Leiden, The Netherlands). The study population consisted of 27 men and 48 women with a mean age at surgery of 47.1 years (15 to 70). The lesions were located in the femur (37, 49%), humerus (24, 32%), tibia (six, 8%), fibula (five, 7%), ulna (two, 3%) and radius (one, 1%). All patients underwent conventional radiography (Table I) and at least two post-operative MRI scans. Independent observers (SHMV, CSvR) retrospectively reviewed all plain radiographs and MRI studies. In case of discrepancy, the two observers discussed the images and reached a consensus view.

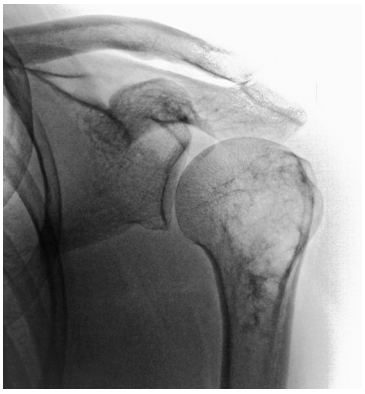

Fig. 1a

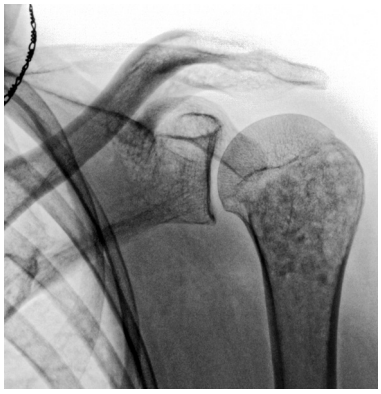

Fig. 1b

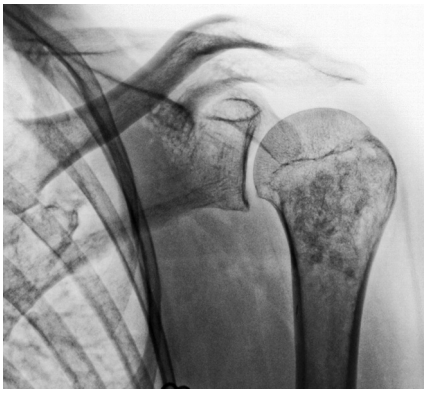

Fig. 1c

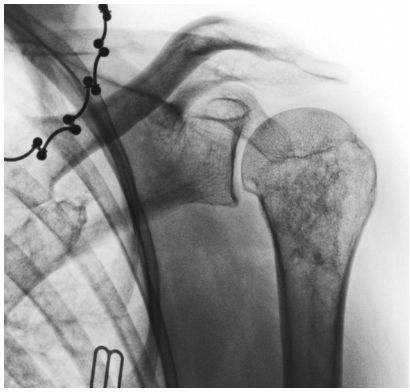

Fig. 1d

Post-operative plain radiographs showing a) lobulated lesion in the proximal humerus metaphysis of the left arm. The lesion is predominantly lytic with some chondroid mineralisation in the distal part. The cortex seems intact. Histological examination after curettage showed ACT/grade I chondrosarcoma. b) Two months after curettage showing the bone graft. No post-operative complications; c) six months after curettage shows early incorporation of the bone graft; d) 24 months after curettage shows further incorporation of the bone graft.

A second procedure was carried out when local recurrence was suspected on MRI during follow-up. Local recurrence was treated by radiofrequency ablation (RFA) if the lesion was over 10 mm in diameter or by further intralesional curettage, phenol and bone grafting if it was 10 mm or less.

Radiology. Plain radiographs were obtained in two planes. The images were reviewed to evaluate the degree of consolidation of the bone window, the extent of incorporation of the bone graft and to assess any signs suggestive of local recurrence or residual disease (e.g. increasing focal radiolucent areas or mineralisation of the chondroid matrix).

The MRI studies consisted of standard T1- and T2-weighted fat-suppressed images, dynamic contrast-enhanced images and static late contrast-enhanced T1-weighted images with fat suppression. All were acquired on a Philips 0.5T (T5-II; Philips Medical Systems, Best, The Netherlands) or a 1.5T (NT; Philips Medical Systems) MR system using a surface coil.

We assessed the appearance of any areas of enhancement in the treated region within the medullary cavity and the degree of consolidation of the bone window. We recorded any change in enhancement, the extent of post-operative oedema and the presence of any new lesion suggesting recurrence of the chondrosarcoma.

Results

All patients had at least two post-operative MRIs (2 to 8). The mean time to follow-up was 70 months (8 to 169). A second procedure was undertaken in 14 patients in whom there was radiological suspicion of residual or recurrent tumour. Of these, eight underwent curettage and five RFA. One patient underwent total knee arthroplasty (TKA) ten years after curettage of an ACT of the distal femur. During surgery, a biopsy was taken but histology of the tissue obtained was inconclusive (Table II, patient 2).

Histological examination was performed on the fine needle biopsy material taken during the RFA session or on tissue obtained by curettage. Unfortunately, no histological biopsy was carried out during RFA in two cases (Table II, patients 4 and 7). Histological examination confirmed recurrence in six cases and was negative in five.

Radiography. Complete consolidation of the bone window was seen in all patients. Two patients suffered a fracture of the femur through the bone window within six weeks of

Table III. MR imaging patterns

Group	Patterns
Group I	Normal appearance of the bone graft without suspicion of residual or recurrent tumour on all post-operative MRIs.
Group II	Nodules within the granulation zone on post-operative MRI, diminishing in size during follow-up.
Group III	Nodules within the granulation zone on post-operative MRI, stable or increasing in size during follow-up.
Group IV	Initially normal appearance of the bone graft on post-operative MRI. Development of a new enhancing lesion suspicious of local recurrence during follow-up.

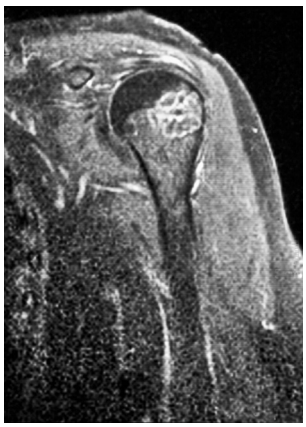

Fig. 2a

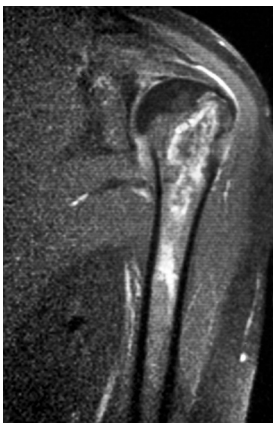

Fig. 2b

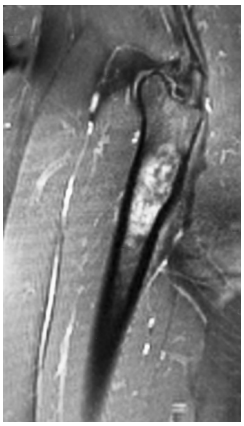

Fig. 3a

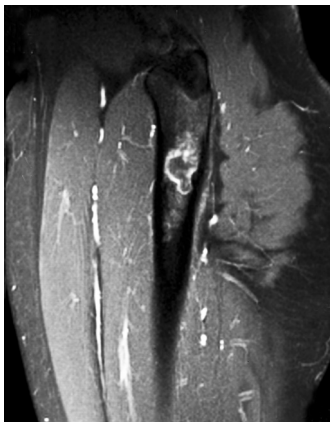

Fig. 3b

MR imaging pattern of group III in a 15-year-old girl with an ACT/grade I chondrosarcoma of the proximal femur. Sagittal T1-weighted MR images after intravenous contrast administration and fat-suppression; a) first MRI carried out seven months after curettage. The marrow cavity in the proximal femur shows marked and inhomogeneous enhancement, which could represent extensive granulation tissue, however small residual nodules cannot be excluded. b) Six months after previous MR examination demonstrates a well-circumscribed lesion with a typical ring enhancement pattern consistent with a recurrence. The enhancing granulation zone/tissue is markedly reduced. Repeated curettage was undertaken: histological examination showed ACT/chondrosarcoma grade I.

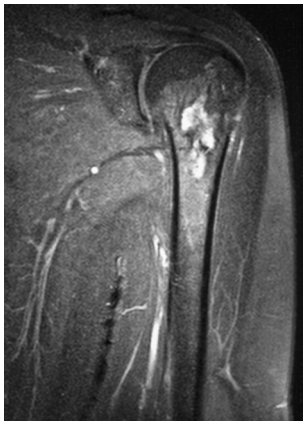

Fig. 2c

Group I lesion: residual nodules, which diminish in time in a 46-year-old woman with an ACT/grade I central chondrosarcoma of the left proximal humerus; a) coronal T1-weighted MR imaging after gadolinium enhancement and fat suppression at diagnosis; ring-and-arc enhancement of a cartilage tumour; b) six months after curettage, the bone graft is surrounded by an enhancing zone of granulation tissue with some soft-tissue oedema at the bone window. Areas of hyperintensity persist. c) Incorporation of the bone graft, decreasing in size. No separate cartilaginous nodules suspicious of local recurrence. Areas still enhance with gadolinium, but decrease in size

curettage. Gradual incorporation of the bone graft was seen in two to five years in all patients (Fig. 1). However, in some patients, there were small radiolucent defects in the bone graft which remainedvisible on serial follow-up radiographs, without increasing in size. No patients showed any sign of local recurrence on plain radiographs.

MR imaging. The recognition of a number of characteristics on the post-operative images which were false positive predictors of recurrence led us to formulate the four risk groups as shown in Table III. We identified four different imaging patterns:

I. A small enhancing rim of granulation tissue around the area of the bone graft. This area becomes smaller with time and the surrounding bone marrow oedema recedes. No residual or recurrent enhancing nodules suspicious of ACT/chondrosarcoma grade I (Fig. 2).

II. Nodules in or around the bone graft. The granulation zone is not well-defined. The nodules diminish in size on follow-up MRIs.

III. Nodules are seen in or around the bone graft. They are stable or increase in size during follow-up MRIs (Fig. 3).

IV. A small enhancing rim of granulation tissue around the area of the bone graft is seen on the first post-operative MRI consistent with the normal appearance of the bone graft. New enhancing nodules develop in the treated region, which are suspicious for local recurrence during follow-up MRI (Fig. 4).

Combining these factors resulted in the proposed flowchart for follow-up and treatment Figure 5. Soft-tissue oedema around the bone window was frequently seen on

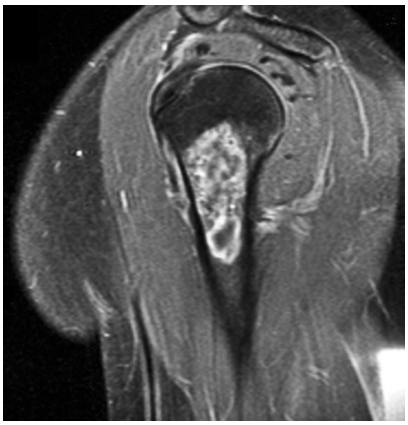

Fig. 4a

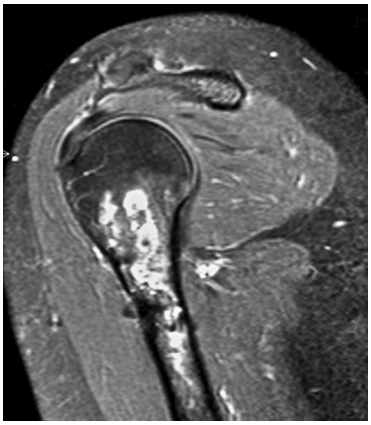

Fig. 4b

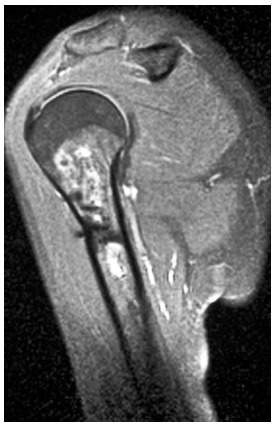

Fig. 4c

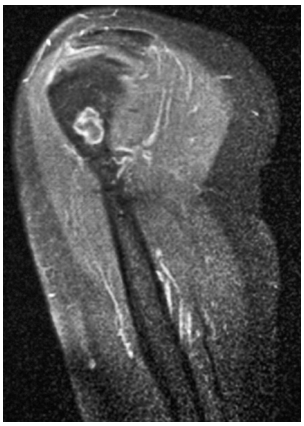

Fig. 4d

MR imaging pattern of group IV with a local recurrence 61 months after initial surgery in a 39-year-old woman with ACT/grade I chondrosarcoma in the right proximal humerus. Oblique T1-weighted MR images after intravenous contrast administration with fat-suppression; a) pre-operative MRI demonstrates the typical enhancement pattern consistent with a cartilage tumour; b) post-operative MRI, 12 months after treatment demonstrates irregular enhancement of the marrow cavity; c) post-operative MRI, three years after treatment demonstrates further resorption or incorporation of the bone graft mimicking small cartilage nodules; d) post-operative MR image, five years after treatment demonstrates a well-circumscribed lesion with a typical ring enhancement pattern consistent with a local recurrence. Histological examination confirmed ACT/grade I chondrosarcoma.

the first post-operative MRI, which lessened in time on follow-up MRI (Fig. 6). Overall, 40 patients (54%) had a pattern of imaging consistent with normal post-operative appearances (group I) (Fig. 2). There were 18 patients (24%) classified as group II. In this group one patient was treated by further curettage: histots (17%) with a pattern of imaging consistent with group III (Fig. 3) and four patients (5%) consistent with group IV (Fig. 4).

Discussion

It is important that patients who undergo intralesional surgery for an ACT/grade I central chondrosarcoma are reviewed because there is a risk that the lesion will develop into a grade II or III chondrosarcoma, and a small risk of dedifferentiation.

We identified four groups of imaging features and designed a flowchart (Fig. 5) which gives recommendations for follow-up imaging.

As our first patients were treated in 1994, the threshold for a second procedure was low because knowledge of the frequency of recurrence and clinical behaviour was limited. With our current knowledge, we would not have treated 'patient 1' in imaging pattern group II (Table III). MRI showed an ill-defined granulation zone which contained some nodules. These decreased slightly in size on a follow-up MRI but, because we suspected residual local disease, the patient underwent repeated curettage despite there being no sign of malignancy on histological examination.

Post-operative radiographs have proved to be of importance in the detection of early complications linked to the surgery, such as fissures, fractures or large residual areas of calcification. However, in this study, plain radiographs failed to detect any of the local recurrences.

There were 13 (17%) planned re-interventions. One patient had a second biopsy during a TKA (Table II, patient 2). However, histological confirmation of residual or recur-

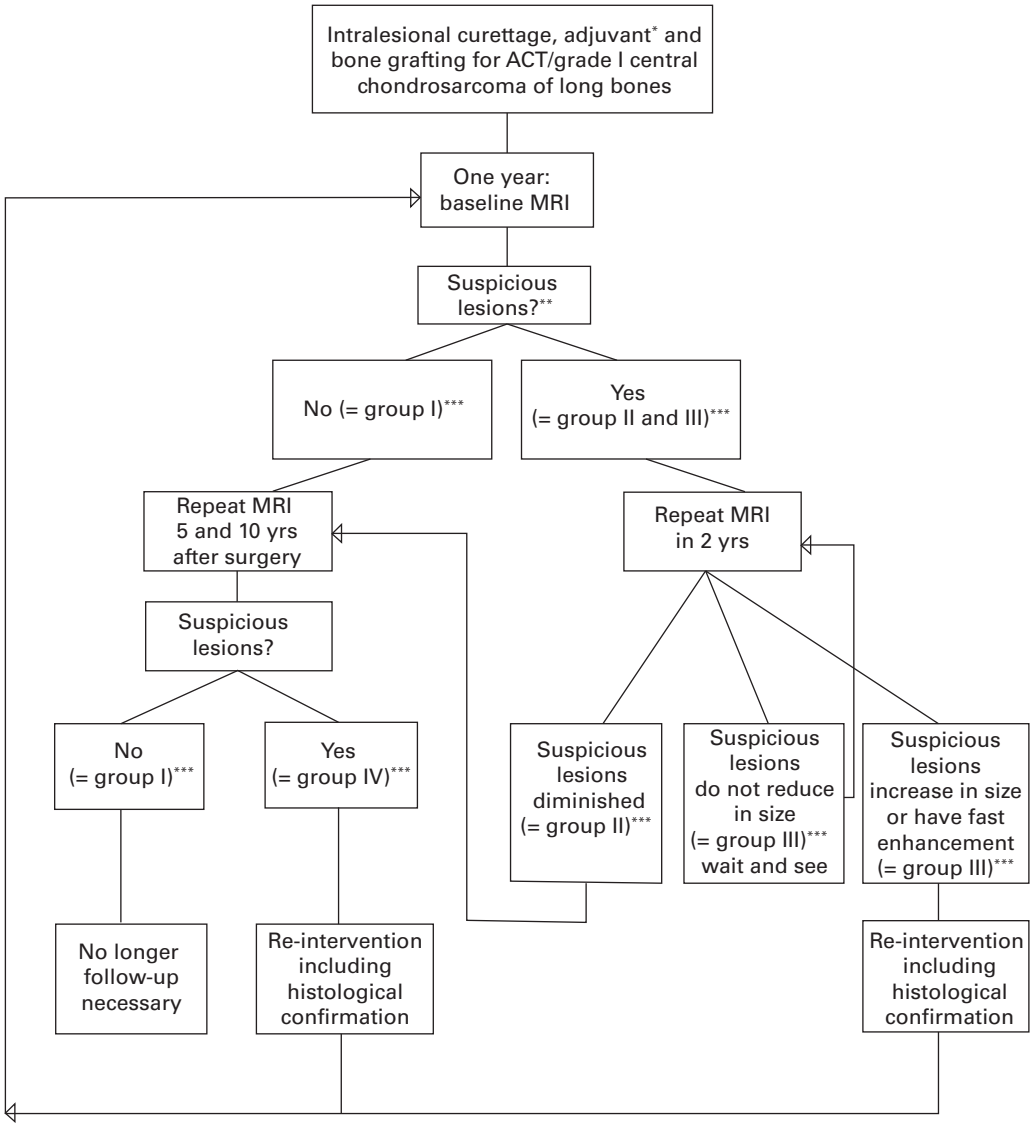

Fig. 5

Flowchart recommending a sequence of follow-up for patients after intralesional treatment for an atypical cartilaginous tumour (ACT)/grade I chondrosarcoma of a long bone.
*as adjuvant, Radio Frequency Ablation, phenol or cryosurgery can be used
**enhancement of nodules within the granulation zone
***Group I: Normal aspect of the bone graft without suspicion for residual or recurrent tumour on all post-operative MR images. Group II: Nodules within the granulation zone on post-operative MR imaging, diminishing in size during follow-up. Group III: Nodules within the granulation zone on post-operative MR imaging, stable or increasing in size during follow-up or fast enhancement of the nodules. Group IV: Normal aspect of the bone graft on post-operative MR images. Development of a new enhancing lesion suspicious for local recurrence during follow-up.

rent tumour was made in only six patients (8%), three in group III patients and three in group IV. Unfortunately, in two patients in the RFA group, no biopsy was taken. No upgrading or dedifferentiation of the cartilaginous tumour was seen on recurrence. In five patients, there was no sign of tumour recurrence or the volume of tissue acquired was too small to make a definite diagnosis. In recent years, improvements in the design of biopsy needles, sampling technique and the expertise of radiologists have developed in concert with oncological and quality control guidelines: these emphasise the need for adequate biopsy before percutaneous RFA is undertaken in the same session.[14]

The surgical field was carefully examined on post-operative MRI. In each patient, we noted that bone graft had a signal intensity which was more or less comparable with normal bone marrow and was surrounded by a zone of variable thickness. This zone showed predominantly high signal intensity on T2-weighted fat suppressed images and enhanced on the late static contrast-enhanced MR images. It consisted of granulation tissue as a fibrovascular reaction of the host to the allograft bone chips in combination with the necrotising effect of the applied phenol. On the first post-operative MRI (about six months after surgery) it can, therefore, be difficult to recognise small resid-

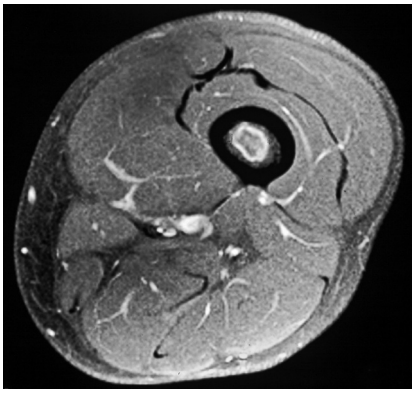

Fig. 6a

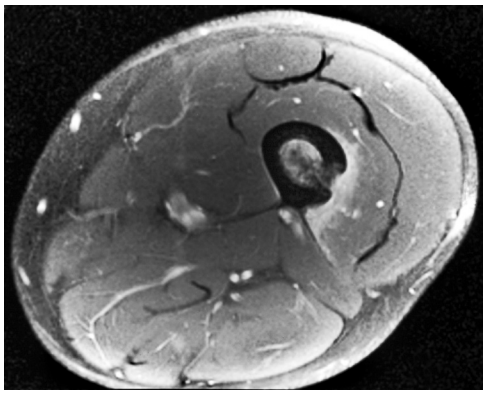

Fig. 6b

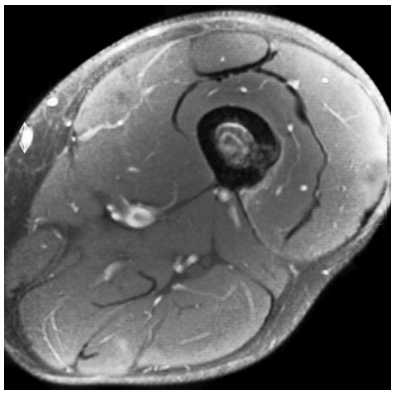

Fig. 6c

Axial MR images of early post-operative changes showing a 31-year-old man with an ACT/chondrosarcoma grade I in the left distal femur. Axial T1-weighted MR images after intravenous contrast administration with fat-suppression through the same position on different time-points; a) the lesion shows typical peripheral ring enhancement; b) the patient has been treated by curettage through a lateral approach. There is marked enhancement surrounding the bone window six months after treatment. The bone window is partially consolidated and shows reactive periosteal and soft-tissue oedema; c) complete consolidation and incorporation of the bone graft 24 months after surgery

ual nodules of chondroid tumour because they have similar imaging features to granulation tissue, however well demarcated. If the enhancing nodules persist (MRI pattern group III) or if new enhancing nodules develop (MRI pattern group IV) then local recurrence of residual tumour needs to be considered. Depending on the size, location and patient-related factors like age, comorbidity and daily activity a wait-and-see policy can be considered or further treatment (RFA or intralesional curettage) may be undertaken.

Moreover, the bone graft used for filling the defect in the marrow cavity after curettage may contain cartilage chips from any residual articular surface present within the bone graft. This may lead to a false-positive interpretation of residual foci of chondroid tissue: however, these will not increase in size over time.

The dynamic contrast-enhanced MR images have the potential to be very helpful in differentiating recurrent disease from granulation tissue on follow-up MRI. However, in our patients, the diagnosis of recurrent disease was suggested by the morphological criteria described in Table III. In our patients, the dynamic contrast-enhanced sequence was of poor quality or not performed in the correct area of interest as MRIs carried out on the 0.5 T MR systems could only include two slices through the area of interest.

Based on the recurrences we have seen and the MRI patterns we have identified, we recommend managing these patients as shown in Figure 5. We are convinced that curettage combined with an adjuvant and bone grafting is a safe and a well-received procedure for patients with a central ACT/chondrosarcoma grade I. When follow-up is carried out according to the proposed schedule, any local recurrence can be detected accurately and in a safe interval.

Take home message:

In the post-operative follow-up for patients treated for an ACT/grade I chondrosarcoma of long bones by curettage and adjuvant, Gd-MRI is the benchmark.

Author contribtions:
S. H. M. Verdegaal: Design of the study, Data collection, Data analysis, Writing paper.
C. S. van Rijswijk: Data analysis, Writing paper.
H. F. Brouwers: Data collection.
P. D. S. Dijkstra: Performed surgeries, Writing paper.
M. A. J. van de Sande: Performed surgeries, Writing paper.
P. C. W. Hogendoorn: Design of the study, Data analysis, Writing paper.
A. H. M. Taminiau: Design of the study, Performed surgeries, Data analysis, Writing paper.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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References

1. **Fletcher CDM, Bridge JA, Hogendoorn P, Mertens F.** *WHO classification of Tumours of Soft Tissue and Bone.* Fourth ed. Lyon: IARC Press, 2013:264–268.
2. **Unni KK, Inwards CY.** *Dahlin's bone tumors: general aspects and data on 11,087 cases.* Sixth ed. Philadelphia: Lippincott, 2006.
3. **Bovée JV, van der Heul RO, Taminiau AH, Hogendoorn PC.** Chondrosarcoma of the phalanx: a locally aggressive lesion with minimal metastatic potential: a report of 35 cases and a review of the literature. *Cancer* 1999;86:1724–1732.
4. **Brown MT, Gikas PD, Bhamra JS, et al.** How safe is curettage of low-grade cartilaginous neoplasms diagnosed by imaging with or without pre-operative needle biopsy? *Bone Joint J* 2014;96-B:1098–1105.
5. **van der Geest IC, de Valk MH, de Rooy JW, et al.** Oncological and functional results of cryosurgical therapy of enchondromas and chondrosarcomas grade 1. *J Surg Oncol* 2008;98:421–426.

6. **Verdegaal SH, Brouwers HF, van Zwet EW, Hogendoorn PC, Taminiau AH.** Low-grade chondrosarcoma of long bones treated with intralesional curettage followed by application of phenol, ethanol, and bone-grafting. *J Bone Joint Surg [Am]* 2012;94-A:1201–1207.
7. **Verdegaal SH, Hartigh Jd, Hogendoorn PCW, Brouwers HF, Taminiau AHM.** Phenol levels during intralesional curretage and local adjuvant treatment of benign and low-grade malignant bone tumours. *Clin Sarcoma Res* 2012;2:10.
8. **Verdegaal SH, Corver WE, Hogendoorn PCW, Taminiau AHM.** The cytotoxic effect of phenol and ethanol on the chondrosarcoma-derived cell line OUMS-27: an in vitro experiment. *J Bone Joint Surg [Br]* 2008;90-B:1528–1532.
9. **Geirnaerdt MJ, Bloem JL, Eulderink F, Hogendoorn PC, Taminiau AH.** Cartilaginous tumors: correlation of gadolinium-enhanced MR imaging and histopathologic findings. *Radiology* 1993;186:813–817.
10. **Geirnaerdt MJ, Hermans J, Bloem JL, et al.** Usefulness of radiography in differentiating enchondroma from central grade 1 chondrosarcoma. *AJR Am J Roentgenol* 1997;169:1097–1104.
11. **Geirnaerdt MJ, Hogendoorn PC, Bloem JL, Taminiau AH, van der Woude HJ.** Cartilaginous tumors: fast contrast-enhanced MR imaging. *Radiology* 2000;214:539–546.
12. **De Beuckeleer LH, De Schepper AM, Ramon F, Somville J.** Magnetic resonance imaging of cartilaginous tumors: a retrospective study of 79 patients. *Eur J Radiol* 1995;21:34–40.
13. **Eefting D, Schrage YM, Geirnaerdt MJ, et al.** Assessment of interobserver variability and histologic parameters to improve reliability in classification and grading of central cartilaginous tumors. *Am J Surg Pathol* 2009;33:50–57.
14. **ESMO/ European Sarcoma Network Working Group.** Bone sarcomas: ESMO Clinical Practice Guidelines for diagnosis,treatment and follow-up. *Ann Oncol* 2014;25(Suppl 3): iii113–123.