Wait- and- scan: an alternative for curettage in atypical cartilaginous tumours of the long bones

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■ ONCOLOGY

Wait-and-scan: an alternative for curettage in atypical cartilaginous tumours of the long bones

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Aims

Due to its indolent clinical behaviour, the treatment paradigm of atypical cartilaginous tumours (ACTs) in the long bones is slowly shifting from intralesional resection (curettage) and local adjuvants, towards active surveillance through wait-and-scan follow-up. In this retrospective cohort study performed in a tertiary referral centre, we studied the natural behaviour of ACT lesions by active surveillance with MRI. Clinical symptoms were not considered in the surveillance programme.

Methods

The aim of this study was to see whether active surveillance is safe regarding malignant degeneration and local progression. In total, 117 patients were evaluated with MRI assessing growth, cortical destruction, endosteal scalloping, periosteal reaction, relation to the cortex, and perilesional bone marrow oedema. Patients received up to six follow-up scans.

Results

At the time of the first follow-up MRI, 8% of the lesions showed growth (n = 9), 86% remained stable (101), and 6% decreased in size (n = 7). During the third follow-up, with a mean follow-up time of 60 months (SD 23), 24 patients were scanned, of whom 13% had lesions that had grown and 13% lesions that had decreased in size. After 96 months (SD 37), at the sixth follow-up MRI, 100% of the lesions remained stable. None of the lesions showed malignant progression and although some lesions grew in size (mean 1 mm (SD 0.8)), no malignant progression occurred.

Conclusion

We conclude that active surveillance with MRI is safe for ACTs in the long bones in the short- and mid-term follow-up.

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Introduction

Chondrosarcomas (CS) are the second most common primary bone tumours.[1] Over the last decade, the incidence of CS grade I has significantly increased to nine per million cases, largely due to an increase in MRI examinations, although the incidence of high-grade CS has not changed.[2] The majority of cartilage tumours are CS grade I, which have been designated by the WHO since 2013 as "atypical cartilaginous tumours" (ACTs).[3] In an updated World Health Organization (WHO) classification published in 2020, the terminology was further adjusted and ACTs were specified for the limbs (appendicular skeleton), whereas CS grade I were designated as lesions in the axial skeleton.[4] These ACTs can be locally aggressive but rarely metastasize.[2,5,6]

Because of their indolent behaviour, the treatment of ACTs has evolved over the past decade. While in the past the majority of these tumours were treated with radical resection, they are now usually treated with curettage in combination with local adjuvant therapy or, alternatively, a 'wait-and-scan' policy with interval MRI scans. Unfortunately, no international consensus exists, and treatment varies per country.[7–10]

A Dutch series of 119 ACT patients treated with curettage and local adjuvant showed promising

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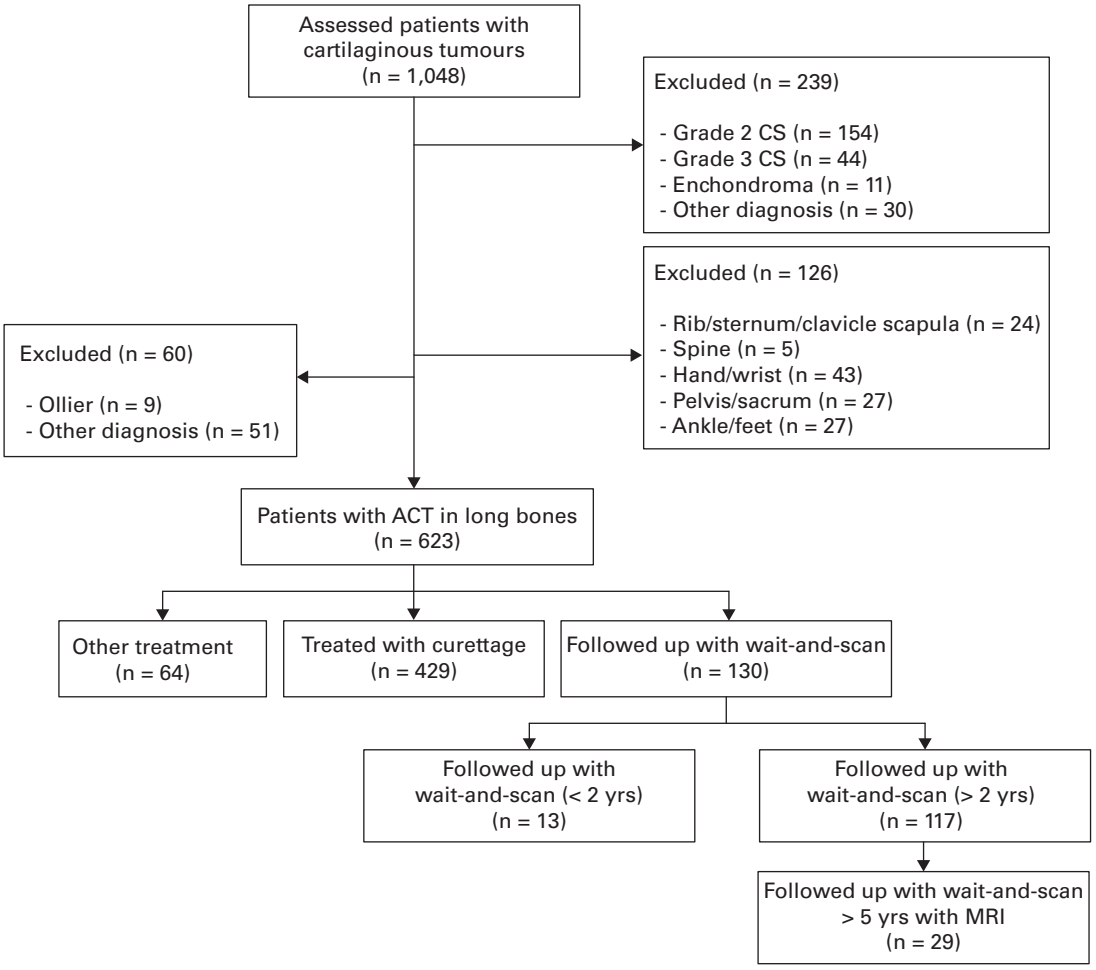


Fig. 1

Flow diagram of the study participants. ACT, atypical cartilaginous tumour; CS, chondrosarcoma; FU, follow-up. Other treatment = radiofrequency ablation or en bloc resection.

results with a small chance of recurrence (3%).[11] However, surgery can lead to complications such as infection, fracture, thromboembolic events, and reoperation due to other reasons than disease progression. A recent review showed that complications occurred in 4% of patients treated with intralesional curettage, mainly due to fracture and infection.[12] Because of these surgical complications, wait-and-scan follow-up may be an alternative. There is, however, still little evidence for wait-and-scan of ACTs regarding safety and long-term outcome.

A retrospective study with 128 patients with enchondromas/ACTs showed that within two years of follow-up, 4% of patients underwent surgical treatment. The reasons for surgical treatment were lesion change, pain, and osteoarthritis. In 51% of the patients tumours remained stable (n = 65), and in 36% tumours showed regression (n = 46). However, only 13% of tumours showed growth (n = 17), of which none developed the characteristics of high-grade CS.[9] Another retrospective analysis of patients with enchondroma/ACT with a mean follow-up of 82 months included 153 patients followed up with wait-and-scan, where surgery was not found to be superior to wait-and-scan with MRI.[13] Neither study distinguished ACT from enchondroma. Distinction between the two entities remains a topic of discussion among radiologists, and there has been a paradigm shift, leading towards greater focus on differentiation of high-grade CS versus ACT/enchondroma.[6,14]

In this study, we hypothesize that interval MRI is as safe as curettage treatment regarding malignant progression of ACTs in the long bones. We analyzed MRI characteristics, lesion growth, and the need for secondary surgery. Additionally, we also hypothesized that the largest differences in size and aggressive characteristics shown on MRI, namely endosteal scalloping, cortical destruction, extent of the lesion to the cortex, and perilesional bone marrow oedema, will be found in those patients with the longest follow-up time interval.

Methods

All patients radiologically diagnosed with an ACT in the appendicular skeleton at the outpatient clinic of the LUMC between 2000 and 2019 were included in a retrospective cohort study. In total, 117 of 623 radiologically diagnosed ACTs in the long bones were followed with wait-and-scan policy. The surveillance programme was standardized as follows: MRI was

Table I. Baseline characteristics of patients with radiologically diagnosed atypical cartilaginous tumours in the appendicular skeleton in the wait-and-scan cohort.

Characteristic	Total
Patients, n	117
Male, n (%)	56 (48)
Mean age at diagnosis, yrs (SD)	55 (11)
Size, n (%)	
< 20 mm	14 (12)
20 to 40 mm	55 (47)
41 to 100 mm	45 (39)
> 101 mm	3 (3)

SD, standard deviation.

performed at the time of diagnosis, and afterwards at one year, three years, and five years. The reason that only 117 patients received wait-and-scan is because active surveillance was not the standard treatment in our centre before 2010. Also, patients were excluded if the follow-up time was shorter than two years, if they were diagnosed with Maffucci syndrome or Ollier's disease, if the tumour was located in the axial skeleton, if the lesion size was smaller than 10 mm, or if treatment had occurred in another hospital. High-grade CS (HGCS) (i.e. grade II or higher) were excluded, as well as clear cell CS, mesenchymal CS, myxoid CS, and juxtacortical CS (Figure 1). High-grade chondrosarcomas, on the other hand, are characterized by MRI features such as periostitis, surrounding bone marrow oedema, cortical breakthrough, a soft-tissue mass, or a mucoid component.[15]

This study was approved by the Medical Ethical Review Committee of Leiden, the Hague, and Delft (protocol number G21.160). Patients were identified through the hospital coding registry. Information on patient demographics, diagnostic characteristics, and course of follow-up was retrieved from patient files. All patients had baseline and follow-up MRI scans, at intervals of approximately one year, although large variation existed within the cohort according to clinical practice. From the MRI reports, specific characteristics were extracted and collected at all timepoints. These included cortical destruction, endosteal scalloping, periosteal reaction, extent of the lesion to the cortex, bone expansion, and perilesional bone marrow oedema, as the literature supports these as characteristics pointing towards ACT instead of enchondroma. The smaller lesions, which did not show any relation to the cortex, were excluded, as they were defined as enchondromas and needed no imaging follow-up.[16,17] The largest diameter was reported in mm over time. This was chosen because the literature shows that there is no difference in reproducible feature rates between 2D and volumetric MRI-based texture analysis. Furthermore, the longest diameter is used in daily clinical practice.[18] In addition, a subset of patients with a follow-up MRI of at least five years after baseline were also assessed.

In total, 1,048 patients were screened for eligibility. Of these, 239 were excluded because they were diagnosed with high-grade CS or enchondroma. Additionally, 126 patients were excluded due to axial location, leaving 683 with ACT in the long bones. After excluding patients diagnosed with underlying syndromes such as Maffucci or Ollier's disease, a total of 623 with a radiologically diagnosed ACT remained. From this group, 130 patients were followed up with wait-and-scan, of whom 117 were followed up for more than two years. A total of 29 patients from this selection were followed up for more than five years, with an MRI at each follow-up moment (Figure 1). In this study, 117 patients met the inclusion criteria: 56 males and 61 females with a mean age at diagnosis of 55 years (standard deviation (SD) 11) (Figure 1). Baseline characteristics are shown in Table I and distribution of radiologically diagnosed ACT locations is shown in Figure 2.

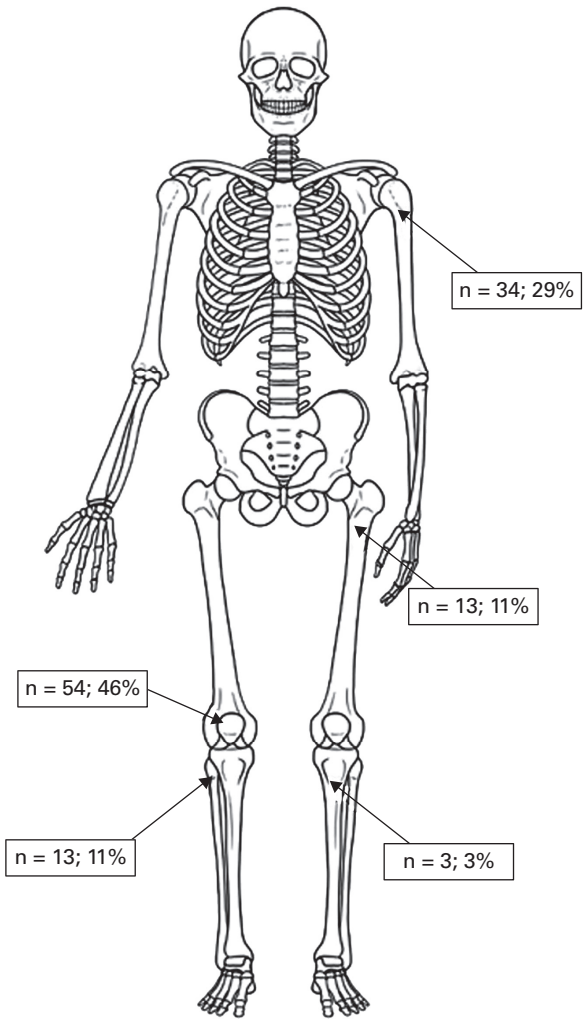


Fig. 2

Locations of radiologically diagnosed atypical cartilaginous tumours in the follow-up cohort of 117 patients.

Statistical analysis. SPSS Statistics v. 25 (IBM, USA) was used to perform statistical analysis. Baseline characteristics were described with their mean (SD) or median (interquartile range (IQR)). SPSS was used to analyze a statistical difference in mean craniocaudal size between the lesions that showed growth versus the ones that did not, using the independent-samples *t*-test with $p < 0.05$ as our significance threshold. Excel v. 16.72.2 (Microsoft, USA) was applied to

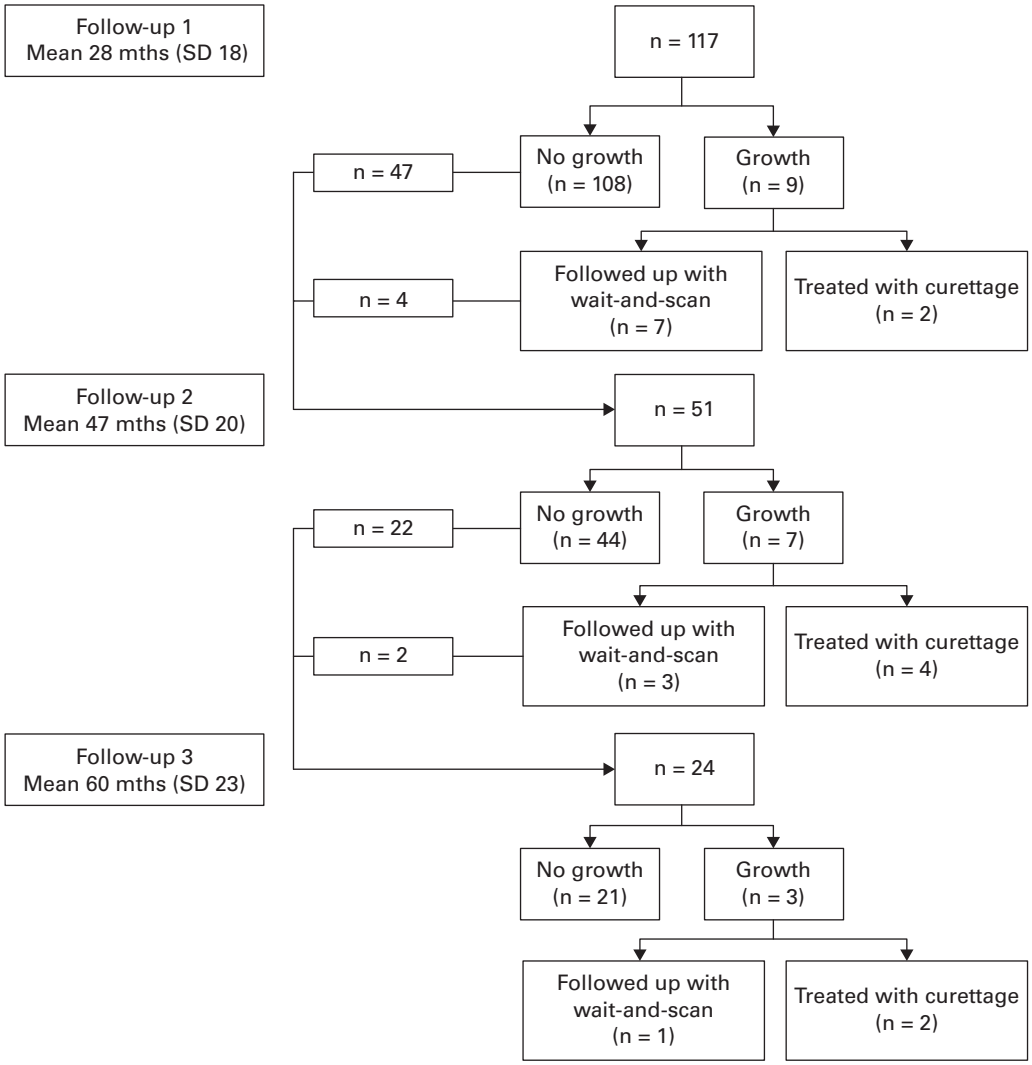


Fig. 3

Flow diagram of MRI follow-up. SD, standard deviation.

Table II. Primary outcome of follow-up (n = 117).

Follow-up moment	MRI at follow-up, n	Mean follow-up from baseline, mths (SD)	Lesions showing growth, n (%)	Lesions showing decrease in size, n (%)
1	117	28 (18)	9 (8)	7 (6)
2	51	47 (20)	7 (14)	5 (10)
3	24	60 (23)	3 (13)	3 (13)
4	12	71 (25)	0 (0)	0 (0)
5	5	97 (30)	0 (0)	0 (0)
6	2	96 (37)	0 (0)	0 (0)

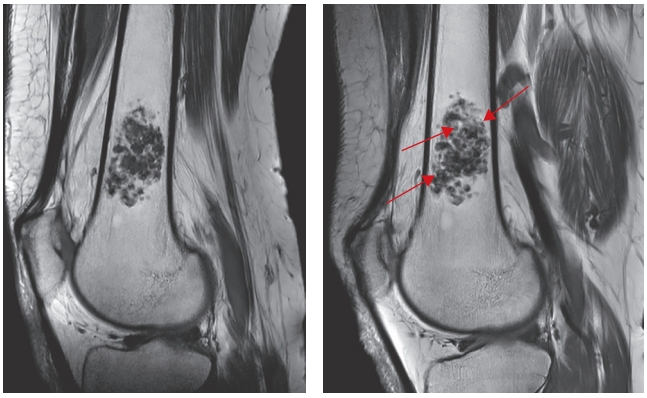
SD, standard deviation.

make a spaghetti plot, providing an illustrative representation of lesion change.

Results

None of the lesions showed bone marrow oedema, bone expansion, or periosteal reaction. Eight patients underwent a diagnostic needle biopsy. In all eight patients, the histopathology confirmed the diagnosis of ACT. In the remaining 109 patients, no biopsy was performed.

Timing of follow-up MRI scans showed a variable pattern. In total, 117 patients had an MRI at baseline and a first follow-up at a mean of 28 months (SD 18). At the first follow-up, nine lesions grew (Table II), resulting in two lesions that were curetted (Figure 3). Lesions grew in seven of 51 patients who had an



a b

Fig. 4

a) Sagittal T1-weighted sequences showing increased fat entrapment over time on MRI. This was performed at baseline, demonstrating a multilocular lesion measuring 5.3 cm in craniocaudal dimension. No cortical scalloping was present. b) Sagittal T1-weighted sequences showing increased fat entrapment over time on MRI after six years, showing no increase in size. Increased interspersed fat was present between the cartilage nodules (see red arrows).

MRI scan at the second follow-up appointment (mean duration of follow-up from baseline 47 months (SD 20)), of which four lesions (in four patients) were curetted. Of 24 lesions, three showed growth on MRI at the third follow-up (mean duration of follow-up from baseline 60 months (SD 23)). Two patients from this group were eventually underwent curettage. Histopathological diagnosis in all curetted lesions (n = 8) confirmed ACT. At the fourth follow-up (n = 12; mean duration 71 months (SD 25)) none of the lesions showed growth or decrease. The same applies to the fifth (n = 5; mean duration 97 months (SD 30)) and sixth follow-up (n = 2; mean duration 96 months (SD 37)). None of the lesions showed malignant progression.

Subgroup analysis of at least five years of follow-up. There were 29 patients with a wait-and-scan follow-up of more than five years (Table III). The mean time of follow-up was 79 months (SD 4). In this group, the median craniocaudal growth was 1 mm (IQR -1 to 3). No statistical difference in mean craniocaudal size was found using the independent-samples *t*-test between the lesions that showed growth (27.6 (SD 11.8)) versus the ones that did not (27.8 (SD 7.4), p = 0.136). The number of patients with scalloping increased in 2/29 cases. Fatty entrapment increased in one patient and extension to the cortex decreased in three patients. Figure 4 shows an example of increased fatty entrapment. Four lesions showed neither growth nor decrease in size. Figure 5 is a spaghetti plot of the behaviour of the lesions in this subgroup. Only the lesions that showed growth or decrease in size over time were plotted (n = 25). Lesion growth generally stabilizes over time; most of the lesions did not grow more than 5 mm. One patient showed 14 mm growth at the follow-up time of five years. This MRI is shown in Figure 6.

Table III. Subgroup analysis: MRI characteristics of 29 patients with at least five years' MRI follow-up.

Characteristic	Baseline MRI	MRI after ≥ five-year follow-up
Size AP, n (%)		
5 to 20 mm	14 (48)	10 (34)
21 to 50 mm	15 (52)	19 (66)
Size LR, n (%)		
5 to 21 mm	20 (69)	16 (55)
21 to 50 mm	9 (31)	13 (45)
Size CC, n (%)		
5 to 21 mm	8 (28)	8 (28)
21 to 50 mm	20 (69)	19 (66)
> 50 mm	1 (3)	2 (6)
Median growth, mm (IQR)		
AP	-	2 (0 to 3)
LR	-	1 (0.5 to 4)
CC	-	1 (-1 to 3)
Scalloping n (%)	13 (45)	15 (52)
< 50% of cortical thickness	10 (34)	12 (41)
> 50% of cortical thickness	3 (10)	3 (10)
Focal scalloping	6 (21)	7 (24)
Extensive scalloping†	7 (24)	8 (28)
Lesion extending to the cortex, n (%)	19 (66)	16 (56)
Wall-to-wall filling, n (%)‡	6 (21)	6 (21)
Fat entrapment, n (%)	23 (79)	24 (83)

*< 10% of 360°.
†> 10% of 360°.
‡In two cases wall-to-wall filling resolved and two cases developed wall-to-wall filling.
AP, anterior-posterior; CC, craniocaudal; IQR, interquartile range; LR, left-right.

Discussion

This study investigated the safety of active surveillance of radiologically diagnosed ACTs in long bones. In total, 117 patients were followed up with an MRI, with up to six scans. Some lesions grew over time, some decreased, but most of the lesions remained stable. This is also reflected in the spaghetti plot of the subgroup analysis: most lesions show no change, and those that grew or decreased, stabilized over time. Most importantly, no malignant progression, developing into a high-grade CS, occurred in our series. From these results, we conclude that wait-and-scan with MRI for ACTs in the long bones can be regarded as safe.

Since the WHO classification changed nomenclature from CS grade I in the long bones to ACT, the approach towards these lesions in our tertiary referral centre, and in other centres, has shifted from curettage to wait-and-scan with MRI.[2–4,9,19] This is because complications and the negative side-effects of surgery make it relevant to evaluate whether active surveillance through wait-and-scan is safe.[13,14,19–22]

Our study has a large series of patients with radiologically diagnosed ACTs and MRI follow-up of up to six times. Furthermore, all MRIs were performed in a tertiary sarcoma centre with a dedicated bone tumour protocol. No adverse advents (i.e. malignant progression) occurred in our study. ACTs may show growth over time, however this does not directly imply malignant progression. Lastly, none of the ACTs showed perilesional bone marrow oedema, periosteal reaction, bone expansion, or cortical destruction, all of which are radiological signs of malignant progression.

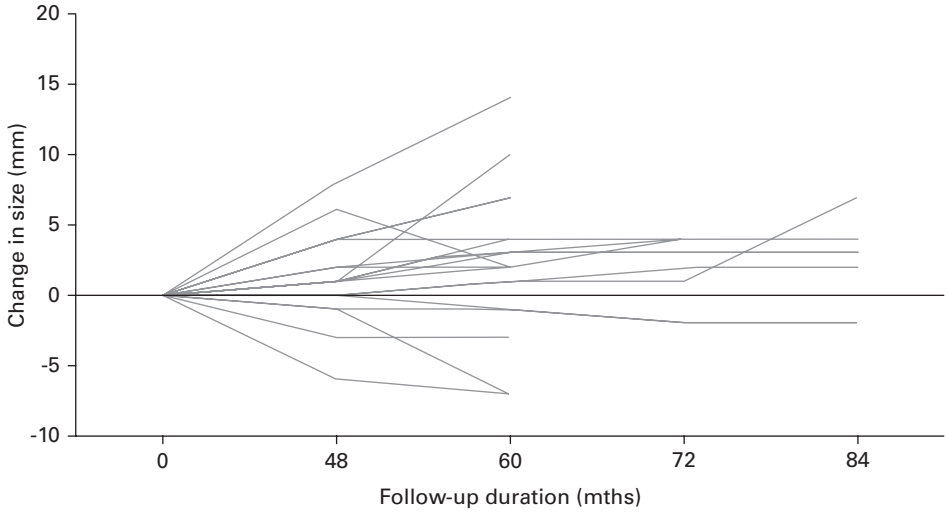


Fig. 5

Spaghetti plot of growth or decrease in size per lesion on MRI in subgroup with follow-up > five years (n = 25). Only the lesions that changed in sized were plotted. In total, four out of 29 lesions remained stable in this subgroup.

A recent Dutch retrospective cohort study investigating active surveillance of enchondromas and ACTs in the long bones supports our findings.[9] A total of 128 patients were followed with MRI, for a minimum interval of 24 months. Of these patients, 13% showed some progression and 87% remained stable or showed regression. Similar to our results, none of the patients developed high-grade CS. In our study, all lesions smaller than 10 mm were excluded. At present, there is no consensus on a clear distinction between enchondroma and ACT, and different size cut-offs exist such as 2 cm up to 5 cm for enchondromas. Part of the lesions in our study have the characteristics of an enchondroma. For this retrospective analysis, we included the patient cohort that was clinically selected for MRI follow-up. Therefore, our study reflects current clinical practice at our tertiary sarcoma centre over the last decade.

As a wait-and-scan policy prevents surgical complications, follow-up of ACT in the long bones through wait-and-scan with MRI is a good alternative to surgery. As Deckers et al[9] also point out, guidelines for wait-and-scan differ greatly among hospitals. In 2019 the Birmingham Atypical Cartilage Tumour Imaging Protocol (BACTIP) criteria were published. These criteria offer guidance for the initial diagnosis, a step-by-step imaging follow-up plan, and indications for tertiary centre referral or discharge from follow-up.[23] Because of the increased incidence in ACTs due to increased application of MRI, an international guideline for follow-up would be useful.[2] However, just as in our study, the BACTIP study lacks data on long-term clinical outcomes after ten or more years. Long-term data are therefore needed to decide how long patients should be followed after the initial diagnosis. Numerous MRI examinations come with a burden of cost and often concern for the patient.[6]

Our study has limitations. Due to changes in the WHO in 2013 with the introduction of the term 'ACT', no clearly specified treatment plan has existed for this tumour.[3] This has resulted in inconsistent decision-making regarding whether curettage or wait-and-scan should be performed. The reasons to choose surgery, such as pain or lesion growth, were often not stated in the clinical records. Pain is often the reason for the MRI, but in general the ACT is not the cause of the pain.[24] Decision-making between active surveillance and curettage was done individually since the change of the WHO definition in 2013. Therefore, argumentation for a specific treatment decision could not always be retrieved from patient records. Indications for surgery for these patients were anxiety, pain, or growth on MRI. However, none of

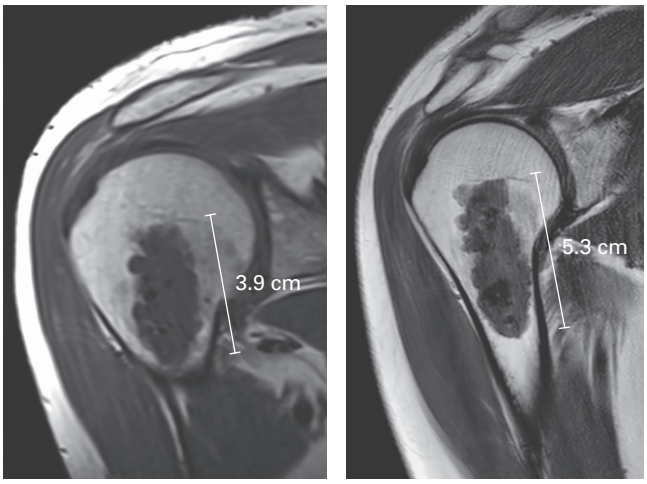


Fig. 6

a) Coronal T1-weighted sequences showing 14 mm growth over time on MRI, at five-year follow-up. This was performed at baseline, demonstrating a lesion measuring 3.9 cm in craniocaudal dimension. b) Coronal T1-weighted sequences showing 14 mm growth over time on MRI at five-year follow-up, showing a lesion of 5.3 cm.

the histology reports showed characteristics of high-grade chondrosarcoma, i.e. the pathology reports confirmed the diagnosis of ACT. The retrospective nature of this study, however, makes it prone to incomplete records. The decision could have relied on the personal opinions and experience of the surgeon and of the patient. Furthermore, the imaging follow-up interval was variable. Finally, treatment bias may have occurred in our data, as shared decision-making was undertaken in this retrospective study and, because this was not standardized in the patient records, we were unable to extract in retrospect the exact reasons for treatment for each individual patient. However, only eight patients underwent surgery in our cohort.

In summary, from our experience in a tertiary sarcoma centre we conclude that active surveillance of radiologically diagnosed ACTs in the long bones with MRI is safe regarding malignant progression in the short- and mid-term follow-up.

Take home message

- From our experience in a tertiary sarcoma centre, we conclude that active surveillance of radiologically diagnosed atypical cartilaginous tumours in the long bones with MRI is safe regarding malignant progression in the short- and mid-term follow-up.

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D. T. Krijvenaar: Data curation.
M. A. J. van de Sande: Conceptualization, Methodology, Resources, Writing – review & editing, Supervision.
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The datasets generated and analyzed in the current study are not publicly available due to data protection regulations. Access to data is limited to the researchers who have obtained permission for data processing. Further inquiries can be made to the corresponding author.

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