Long-term follow-up with MRI scans after enucleation of peripheral nerve schwannomas: results from a single-center case series

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Long-term Follow-up with MRI Scans After Enucleation of Peripheral Nerve Schwannomas: Results from a Single-center Case Series

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BACKGROUND: **Enucleation is a surgical technique to resect peripheral nerve schwannomas. The procedure has a low risk for postoperative deficit, but a small chance for recurrence, because tumor cells may remain inside the pseudocapsule that is left after resection. Magnetic resonance imaging (MRI) scans are frequently performed after surgery to investigate potential residual tumor, but currently there is little information in the literature on the value of follow-up with MRI.**

MATERIAL AND METHODS: **All patients who underwent enucleation of a peripheral nerve schwannoma between October 2013 and June 2022 were included. Postoperative MRI scans (gadolinium-enhanced) made at different time points after the surgery were re-examined for residual enhancement. Patients with residual enhancement were contacted to inform whether symptoms had recurred.**

RESULTS: **A total of 75 schwannoma enucleations in 74 patients were included. The first postoperative MRI scan, performed 3 months after the surgery, showed no residual enhancement in 50 patients. In the remaining 24 patients, another MRI scan was made 1 year after the surgery, which still showed a possible remnant in 11 patients. On the third MRI scan, performed 2 years after enucleation, there were 7 suspected cases (9%). None of these patients had clinical symptoms at a mean postoperative follow-up of 5 years.**

CONCLUSIONS: **Our data show that the value of postoperative MRI scans after enucleation of peripheral nerve schwannomas is limited, because residual enhancement in the beginning can be non-specific and the small percentage of patients, that persistently had a potential remnant, were all asymptomatic.**

INTRODUCTION

Schwannomas are benign peripheral nerve sheath tumors that can occur anywhere along the course of a peripheral nerve. These tumors arise from Schwann cells, which are located around axons and produce myelin. Genetic mutations in Schwann cells may lead to uncontrolled cell division and the development of a focal tumor inside the affected nerve.[1] Schwannomas are often confined to a single fascicle with the normal fascicles located around the lesion. During the formation of the tumor, the outside layer of the fascicle (the perineurium) forms the tumor capsule that separates the tumor from the normal fascicles. Everything outside the capsule is called pseudocapsule, which potentially also contains normal nerve fascicles.[2,3]

Schwannomas may be asymptomatic, but patients can develop symptoms, including local swelling, tenderness, and radiating pain in the sensory distribution area of the affected nerve. There are different treatments options (wait-and-scan, biopsy, or surgical removal).[4] Depending on the severity of these symptoms, and size and location of the tumor, the patient and the surgeon together may decide to surgically remove the tumor. There are several techniques for resection. In toto resection in which the entire affected nerve segment is removed, is only performed in the case of very small sensory nerve branches. The most

Key words
- Peripheral nerve sheath tumor
- Radiologic
- Radiology
- Surgery
- Surgical
- Value

Abbreviations and Acronyms
Fs: Fat suppression
Gd: Gadolinium
HMC: Haaglanden Medical Centrum
MRI: Magnetic resonance imaging

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frequently performed procedures are *enucleation* and *intracapsular resection*.[5-9] These terms are used interchangeably, but an important difference (as described by Stone and Spinner[3]) is that in the enucleation procedure a plane is sought between the pseudocapsule and the true capsule (Figure 1), while in the intracapsular technique the true capsule is opened, which often makes it more difficult to remove the tumor in one piece (because the tumor is soft and easily breaks) and probably is associated with a higher risk for recurrence. Enucleation therefore generally is the preferred technique of schwannoma removal, but, as was recently shown in a histopathologic study by Stone et al., small remnants of tumor may be left inside the pseudocapsule after resection with this technique, which might also lead to tumor recurrence.[2]

In clinical practice it is often standard of care to follow up on patients with magnetic resonance imaging (MRI) after both enucleation and intracapsular resection. There are no specific guidelines for this, but frequently MRI scans are performed somewhere between 3 months to 1 year after the surgery. The role of MRI in postoperative management is still questionable, because when the images show enhancing tissue, it is often unclear whether it is a schwannoma remnant, or postoperative granulation tissue. Moreover, the overall recurrence rate is probably low, based on studies that investigated this for spinal schwannomas (reporting a recurrence rate of 4%–6%).[10-13] In our center, according to local protocol, a standard follow-up MRI with gadolinium is performed 3 months postoperatively to evaluate whether there is postoperative enhancement. In case of a suspected residual tumor, the patient is monitored with sequential MRI scans in time.

In the current literature there is little data on the value of postoperative MRI scans in the follow-up after resection of peripheral nerve schwannomas. Postoperative MRI scans after administration of gadolinium may show focal enhancement due to the disrupted pseudocapsule. This enhancement might be caused by normal postoperative changes (due to inflammation, seroma, and/or edema), and may also be caused by contracted walls of the pseudocapsule. The focal enhancement can thus be non-specific, making it difficult to differentiate between normal postoperative enhancement versus focal enhancement due to residual tumor.

The aim of this article was to retrospectively investigate the results of this postoperative follow-up with MRI scans in a cohort of patients that underwent enucleation of peripheral nerve schwannomas in a single center by a single surgeon.

METHODS

Before the start of this study, approval had been obtained from the medical ethics committee of the Haaglanden Medical Center.

Retrospective chart review was performed on all patients that underwent enucleation of a peripheral nerve schwannoma between October 2013 and June 2022 by the senior author (G.dR.) at the Haaglanden Medical Centrum (HMC). Cases of spinal schwannomas and tumors that had been removed with the originating nerves were excluded. The technique of enucleation is illustrated and described in Figure 1. In short: After identification of the schwannoma and the proximal and distal nerve ends, the surface of the nerve at the area of the tumor was stimulated with a bipolar stimulation probe to identify an area where the nerve could be longitudinally opened without damaging motor nerve fascicles. The pseudocapsule was opened and a plane was sought between the pseudocapsule and the true capsule.[3] The fascicle that entered and exited the tumor was identified. In the absence of a motor response, after bipolar stimulation, this fascicle was transected proximal and distal to the lesion. The lesion was subsequently removed with the true capsule from the pseudocapsule, which in all cases was left in place (was not resected or reduced).

Patient characteristics and preoperative MRI findings (sex, age, location and size of schwannoma) were assembled. Surgical operating notes were reviewed, as well as potential complications during follow-up and clinical examinations. Data on potential loss of sensation and weakness of muscles innervated by the affected nerve were noted. In addition to the clinical follow-up, between June 2023 and March 2024 all patients with a potential remnant on postoperative MRI scan were again contacted by telephone to inform if patients meanwhile had developed symptoms or if patients potentially had been operated elsewhere.

Postoperative MRI Analysis

In all cases of schwannoma enucleation, an MRI scan with gadolinium was made 3 months after the surgery. In case of a suspected residual lesion, the MRI was repeated 6–12 months after the surgery. If the potential residue persisted on the second MRI, another MRI scan was made at 2 years after the surgery. MRI scans were made using a 1.5 Tesla (Siemens, Munich, Germany) scanner at the HMC. According to local protocol, T1, T2fs and T1 after gadolinium sequences were acquired. Between January 2021 and January 2023 all MRI scans (pre- and postoperative) were re-evaluated by musculoskeletal radiologists (E.C. and P.K.) with, respectively, 30 and 15 years of experience. The size of the schwannoma on the preoperative MRI scan was measured as the largest diameter on transverse T1-weighted images after gadolinium. For the postoperative MRI scans, assessment of a potential remnant was based on expected morphologic postoperative changes in combination with T2-weighted and enhancement characteristics.

Limited T2 hyperintensity and enhancement with a diffuse distribution along the operation area and without mass effect at the site of the initial schwannoma was considered as "normal post-perative findings" (Figure 2). In case of persistent (nodular) mass effect in combination with T2 hyperintensity and extensive enhancement, the MRI was scored "undetermined" regarding to persistent remnant or postoperative granulation tissue. If a consecutive MRI showed less enhancement and/or a decrease in mass effect or no mass effect, this MRI was scored as "no remnant" (Figure 3). In these cases, there was no further follow-up with MRI. In case the enhancement was the same as on the first postoperative MRI with no decrease in mass effect, this was scored as a "potential remnant" and another follow-up with MRI was ordered (Figure 4). The size of potential remnant on the last MRI scan was measured in all directions (length and width in 2 directions).

Statistical Analysis

Pearson correlation analysis was performed to investigate potential difference in mean tumor size for the group with and without residual enhancement on the last MRI scan.

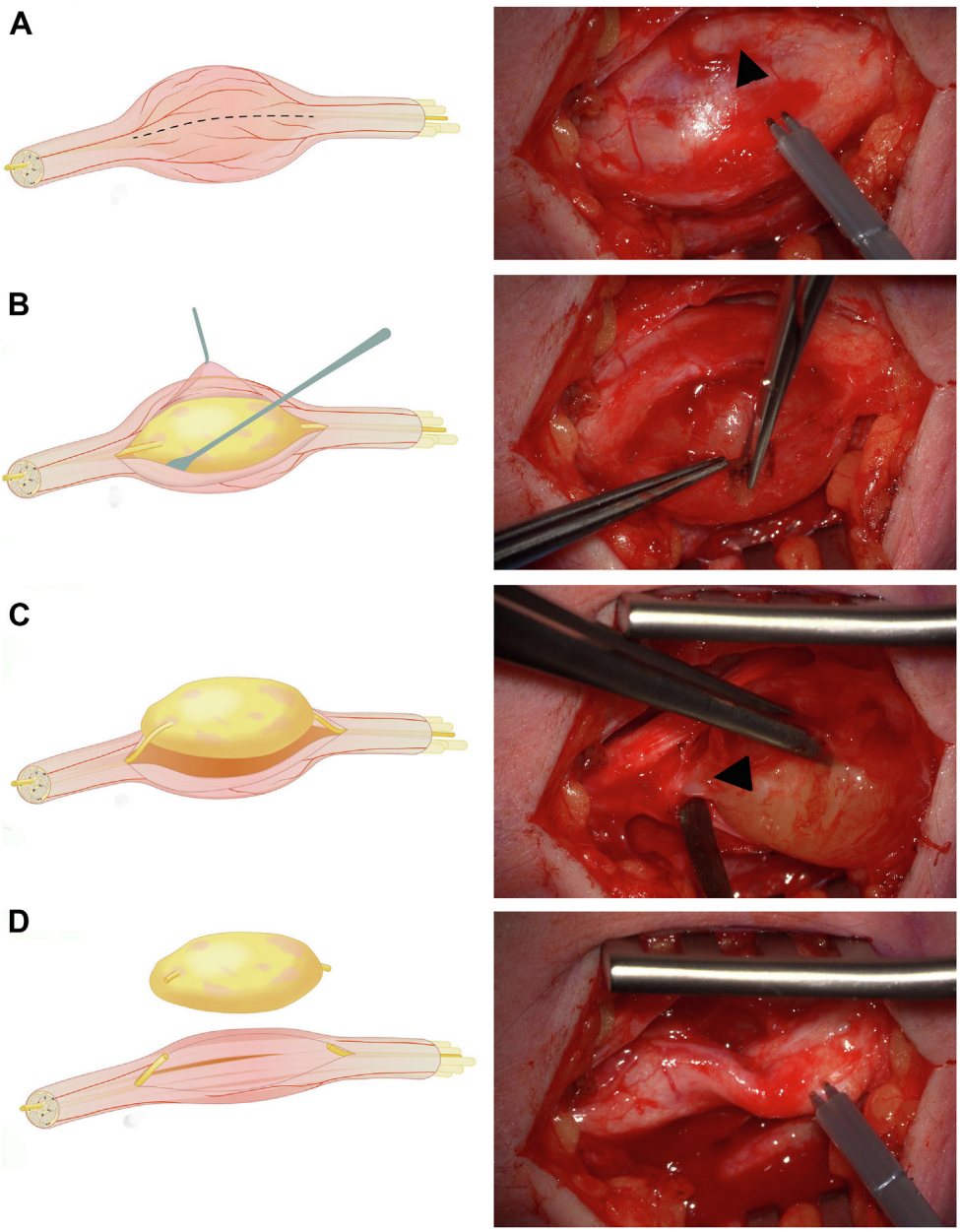

Figure 1. Anatomical drawings and intraoperative pictures to illustrate the technique of enucleation. (**A**) Illustration shows the site (*dashed line*) where the nerve is opened longitudinally over the swelling. Intra-perative picture shows that a site is selected where there is no motor response during stimulation and away from the normal fascicles running along the tumor (*arrowhead*). (**B**) Illustration shows the dissection of the tumor in the place between the true capsule and the pseudocapsule which contains normal fascicles.[3] Intraoperative photograph shows that a site-cut (*sewing dart*) can be made in the pseudocapsule to more easily dissect out the lesion. Care of course should be taken not to damage normal fascicles. (**C**) Illustration shows the proximal and distal fascicle from which the tumor originates. Intraoperative photograph shows the exciting fascicle at the distal site. (**D**) After transection of the proximal and distal fascicles the tumor can be removed, leaving the pseudocapsule in place. Intraoperative picture shows the collapsed pseudocapsule that is stimulated intraoperatively to check for motor function after resection of the tumor.

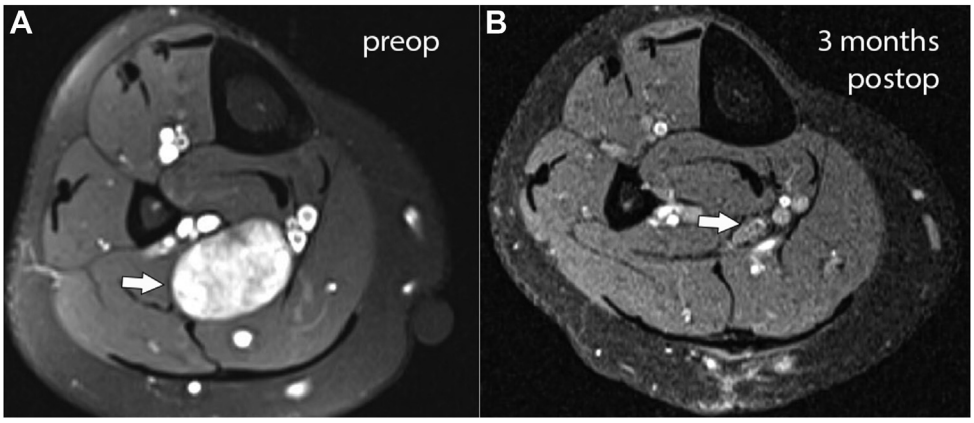

Figure 2. An example of normal postoperative enhancement. Transverse magnetic resonance T1-weighted transverse images with fat suppression after intravenous gadolinium (T1fs+Gd) show (**A**) a diffusely strong enhancing solid lesion (*arrow*) in the course the tibial nerve, and (**B**) 3 months after enucleation, a very limited enhancement at the previous location of the schwannoma (*arrow*) without mass effect (with enhancement in the subcutaneous tissue as well).

RESULTS

This retrospective study consists of a cohort of 75 histopathologically confirmed schwannomas in 74 patients who had undergone an enucleation procedure in the HMC between October 2013 and June 2022. All patients had been followed up with postoperative MRI scans. One patient with schwannomatosis had 2 separate schwannomas in the sciatic nerve. There were no patients with neurofibromatosis. Patient characteristics and locations of schwannomas are provided in **Table 1**. The mean duration of preoperative symptoms was 17 months (range: 3 months to 10 years). The mean size of schwannomas was 2.1 cm (range: 0.6–7.3 cm). In 4 cases a biopsy had been performed prior to surgery to confirm the diagnosis of schwannoma.

Clinical Outcome

The clinical follow-up varied from 3 months to 5 years. Numbness was postoperatively observed in 14 patients (19%), who recovered in many cases (9%) within half a year. Six patients experienced a small area of numbness. Motor weakness (Medical Research Council grade 4) was present in 3 cases directly after surgery (in 2

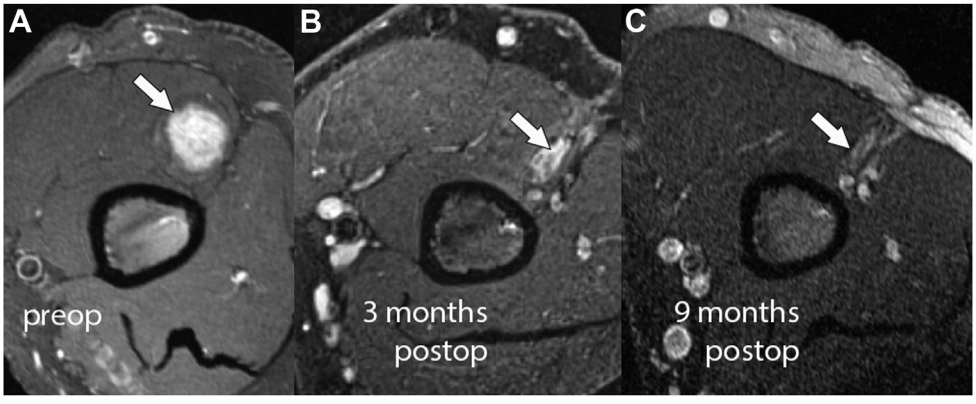

Figure 3. An example of residual enhancement 3 months after the surgery, which had decreased at 9 months after the surgery. (**A**) Transverse magnetic resonance T1-weighted images with fat suppression after intravenous gadolinium (T1fs+Gd) with an enhancing solid lesion (*arrow*) in the course of the radial nerve preoperatively. (**B**) Postoperative enhancement at the resection site 3 months after enucleation with the impression (*arrow*) of limited mass effect (at this time it remains undetermined whether this is a potential remnant). (**C**) Nine months after enucleation, tthe enhancement observed in **B** has decreased ((*arrow*), which suggests that the enhancement at 3 months was caused by a combination of normal postoperative enhancement in a collapsed pseudocapsule.

Figure 4. An example of a suspected remnant with persistent enhancement on postoperative MRIs 3 months, 15 months, and 22 months after the surgery. (**A** and **B**) Magnetic resonance T1-weighted images with fat suppression after intravenous gadolinium (T1fs+Gd) show a heterogenous enhancing solid mass (*arrow*) in the course of the sural nerve. (**C** and **D**) Postoperative consecutive MRIs T1fs+Gd show a small nodular mass at the location of the previously resected schwannoma (*arrow*). (**E-H**) Post-perative enhancement with a small nodular component (*arrow*) remains stable during the follow-up of 22 months.

Table 1. Patient Characteristics and Location of Schwannoma

Patient Characteristics			**n = 74**
Male			36 (49%)
Female			38 (51%)
Age, years			51.5
Location schwannoma	**n = 75**	**Mean Size**	**Range**
Upper extremity	n = 31		
Median nerve	9	1.6 cm	1.0–2.5
Ulnar nerve	10	2 cm	1.0–5.3
Radial nerve	6	1.7 cm	0.7–2.2
Brachial plexus	1	2.0 cm	
Other	5	3.0 cm	1.2–7.3
Lower extremity	n = 40		
Sciatic	6	2.4 cm	1.2–6.4
Tibial	11	2.5 cm	1.0–5.3
Peroneal	9	2.3 cm	1.3–4.0
Other	14	2.0 cm	1.0–6.0
Head/neck			
	3	1.9 cm	1.6–2.4
Trunk			
	1	1.1 cm	

cases the median nerve and in 1 case the peroneal or fibular nerve), which resolved completely in time in all cases. Two other complications occurred: one wound dehiscence and one superficial infection (both treated conservatively). Pain symptoms (if present preoperatively) subjectively decreased in all patients postoperatively.

Postoperative MRI Analysis

In 50 patients (68%) the first follow-up MRI at 3 months showed no signs of a remnant (Figure 5). This included the patient who had 2 separate schwannomas. In each of these cases there was slight enhancement, but this was considered to be consistent with normal postoperative enhancement (an example of which can be seen in Figure 2) according to the criteria described above. Clinical follow-up did not raise suspicion of remnant schwannoma.

In the remaining 24 patients, the first follow-up MRI showed focal enhancement in the resection area of the nerve, which was not diffusely distributed along the pseudocapsule and therefore less suspicious for normal postoperative enhancement. Because of potential residual tumor, a second postoperative MRI scan was ordered in these patients, performed at a mean interval of 12.1 months after surgery. In 1 case, reassessment could not be conducted, because the particular MRI scan had been performed in a foreign center from which it could not be retrieved. In 12 out of these 24 cases (50%) there was a decrease in enhancement and/or

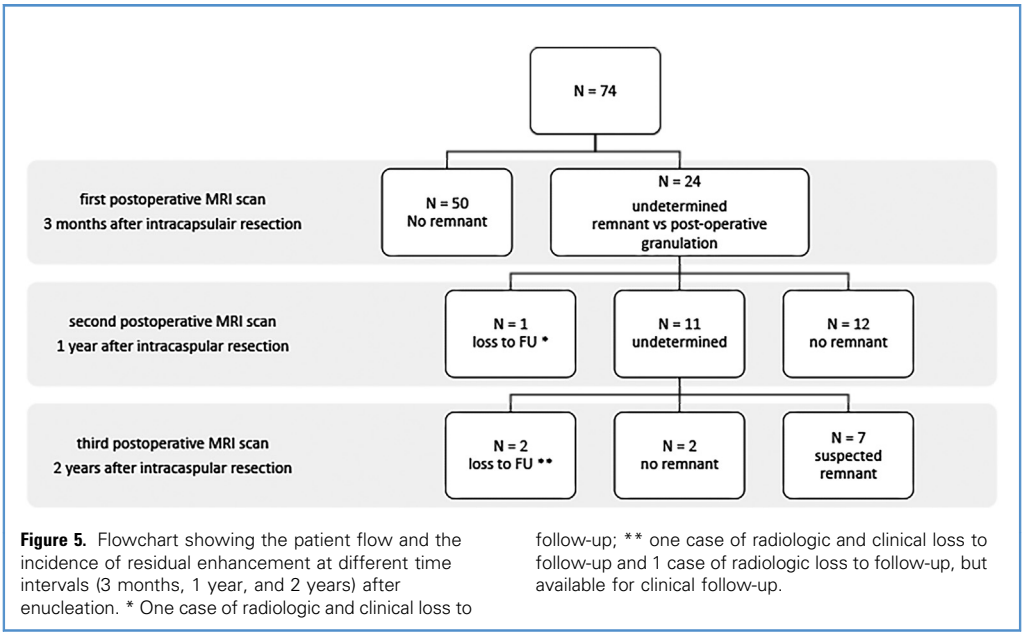

Figure 5. Flowchart showing the patient flow and the incidence of residual enhancement at different time intervals (3 months, 1 year, and 2 years) after enucleation. * One case of radiologic and clinical loss to follow-up; ** one case of radiologic and clinical loss to follow-up and 1 case of radiologic loss to follow-up, but available for clinical follow-up.

mass effect on the second MRI in comparison to the first postoperative MRI scan. On this basis it was assessed that there was no residual tumor (as depicted in Figure 3). In the other 11 cases it remained equivocal whether there was a remnant schwannoma or postoperative granulation tissue based on radiologic imaging. Of these 11 patients, 2 patients were lost to follow-up: 1 patient was also lost to clinical follow-up; the other patient renounced additional scans but was available for clinical follow-up. In the remaining 9 patients, at least 1 more follow-up MRI scan was made 1 year after the second MRI scan provided an indeterminate result. From this group, two patients were ruled out to have signs of remnant schwannoma based on MRI findings. In the remaining 7 patients (with still persistent, non-reducing enhancement comparable to Figure 4), it was decided to only perform additional follow-up MRI scans in case of recurrent symptoms, because these patients did not have recurrence of symptoms. Measurements performed on the latest MRI scans showed a mean diameter of 0.5 and 0.6 cm (measured in 2 planes) and mean length of 2.3 cm (along the course of the nerve). In 1 patient a fourth MRI scan had been made 4 years after the surgery, which still showed a stable size of the residual enhancement. Only in 1 patient the lesion had slightly increased in size during the follow-up. At a mean interval of 5.1 years after the surgery (range: 1.8–9.4 years), all cases with a suspected remnant were contacted by telephone: None of these patients experienced symptoms at the end of the follow-up period.

Statistical comparison of the groups with and without a radiologic residue showed that the mean initial tumor size in the 2 groups (respectively, 2.1 and 2.5 cm in diameter) was not significantly different. The effect of previous biopsy could not be investigated, as only 4 patients underwent a biopsy before surgery and in none of these cases was a potential residue observed.

DISCUSSION

In this study on follow-up with MRI after enucleation of peripheral nerve schwannoma, continuous enhancement was found in 7 out of 75 cases (9%) at a mean of 2 years after the surgery. In none of these patients did this residual enhancement lead to recurrence of symptoms. To the best of our knowledge, this is the first study in which residual enhancement on postoperative MRI scans after enucleation of peripheral nerve schwannoma has been analyzed. Based on the present study and results of several former retrospective studies, the recurrence rate of peripheral nerve schwannoma after enucleation seems to be low. Niepel et al. reported 3 clinically suspected recurrences out of 18 patients with an average follow-up of 50 months.[7] Although patients were reportedly evaluated by MRI to rule out or confirm recurrence of schwannoma, the results of MRI in that study unfortunately were not presented. Oberle et al. reported results for 16 patients, in whom no clinical recurrence was observed, with a mean follow-up of 23 months.[9] In a recent study, Stone et al. investigated the pseudocapsule sent for histopathologic analysis in 36 patients, revealing remnants of tumor in 10 cases. With an average follow-up of 3.1 years in that study, no cases of clinical recurrence were found. Although it is difficult to extrapolate these histopathologic results to the MRI findings in our study, this study thus confirms that even in suspected cases of residual tumor, the chance for clinical local recurrence is low.[3]

Value of Postoperative MRI After Enucleation of Schwannoma

The low chance of clinical recurrence raises the question what the value of a postoperative MRI scan is in the follow-up of patients after enucleation of schwannomas. In our study only in 9% of the schwannomas that had been enucleated was residual enhancement observed on the last MRI scan made 2 years after the surgery,

and none of cases had clinical symptoms at the end of the follow-up period (5.1 years after the surgery). At the first follow-up MRI scan after 3 months, however, in 32% of the patients a focal enhancement was observed on the MRI that could not be differentiated from normal postoperative enhancement and these patients were therefore sent for additional MRI follow-up after 9 months. Although the percentages dropped to 17% after 1 year and 9% after 2 years, the finding of positive enhancement can be concerning to the patient and the extra MRI scans are associated with extra burden and health-care costs.

Our study also shows that it can be difficult to distinguish between normal postoperative enhancement with a diffuse distribution along the operation area and focal enhancement due to residual tumor. The enhancing thickened pseudocapsule seems a normal postoperative finding after resection of schwannomas. This feature might be confusing for a general radiologist, as these characteristics are criteria for residual tumor in other tumor groups. Continuous enhancement at later follow-up periods theoretically could also be caused by (a combination of) postoperative changes and a collapsed pseudocapsule. Interestingly, in the 7 cases that had residual enhancement at the latest follow-up, in 6 cases this mass enhancing nodule was stable over time. Only in 1 case had the enhancement slowly increased over time.

One reason why a postoperative MRI scan could still be of value after enucleation of peripheral nerve schwannomas would be to have a reference scan in case a patient presents with clinical symptoms of recurrence. In that case, the surgeon would know if a small residual tumor was already present on the first postoperative MRI scan. As our study suggests, ideally such a scan should be made at the earliest 1 year after the surgery. Another reason could be if there was difficulty intraoperatively in finding the right plane between the capsule and pseudocapsule or if the capsule was deliberately (for internal debulking) or accidently breached. In case of an uneventful enucleation procedure, however, we do not advocate to follow-up with MRI, because as the results of our study show the finding of residual enhancement has no clinical consequence and raises uncertainty in a relatively high percentage of patients.

Limitations

This study has several shortcomings. First of all, follow-up MRI scans were only performed in cases of residual enhancement suspect for residual tumor. Ideally, all patients should have been followed, and also for a longer period of time, to analyze potential radiologic recurrence in cases without initial postoperative enhancement. A shown by Stone et al.,[2] small remnants of tumor are frequently present in the pseudocapsule that is left in place and these depositions may lead to recurrent enhancement in time. Second, it should be noted that enucleation possibly was not completely achieved with an intact true capsule around the entire lesion as previously described by Stone and Spinner.[3] As stated by these authors, the intracapsular technique probably leads to a higher chance for remnants, because the tumor is soft and easily breaks. Although the inside of the pseudocapsule, after enucleation of the schwannoma, was inspected in the present study in all cases, possible small remnants may have been left inside this capsule in some cases. The shape of the residual enhancement with a relatively larger length (2.3 cm) compared with the diameter (0.5–0.6 cm) suggests that this enhancement was present in the entire pseudocapsule rather than in focal lesion inside the pseudocapsule, although more research is needed to further investigate this.

Third, the mean size of schwannomas in our study (2.1 cm) was relatively small compared with the mean size reported by Date et al. (3.2 cm).[14] This could be due to difference in referral patterns and/or affected nerves. Possibly a larger tumor has a higher chance of recurrence, because the true capsule has to be opened to internally debulk the tumor before it can be safely removed from the surrounding nerve fascicles. This internal debulking may have an impact on the potential for complete resection, because in these cases it might be more difficult to find the right place between the pseudo and true capsule. The same goes for cases that previously underwent a biopsy, which more frequently is performed in larger schwannomas (>3 cm). Although in the 4 cases in which biopsy had been performed in our study, no residual enhancement was observed on follow-up MRI.

CONCLUSIONS

Our data suggest that postoperative MRI scans have a limited value in the follow-up of patients after enucleation of peripheral nerve schwannomas. Especially within the first 3 months after surgery, nonspecific enhancement at the resection site may be present. In our study, only 9% of the patients had residual stable enhancement on MRI 2 years after enucleation, which could be either normal enhancing postoperative tissue or residual tumor. None of these patients experienced recurrence of symptoms at a mean follow-up of 5.1 years after the surgery, rendering the clinical relevance of positive MRI findings low. If standard follow-up with MRI is desired, our study shows that it can best be performed 1 year after the surgery. Another reason could be if the capsule is breached intraoperatively, which increases the risk for a local remnant.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

F. Laura ten Hove: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Isabeau A. Ciggaar:** Writing – review & editing, Writing – original draft, Investigation, Formal analysis. **Emile G. Coerkamp:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Data curation. **Peter R. Kornaat:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Formal analysis. **Godard C.W. de Ruiter:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization.

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