



The role of MRI and ultrasound imaging in Morton's neuroma and the effect of size of lesion on symptoms

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We investigated 29 cases, diagnosed clinically as having Morton's neuroma, who had undergone MRI and ultrasound before a neurectomy. The accuracy with which pre-operative clinical assessment, ultrasound and MRI had correctly diagnosed the presence of a neuroma were compared with one another based on the histology and the clinical outcome.

Clinical assessment was the most sensitive and specific modality. The accuracy of the ultrasound and MRI was similar and dependent on size. Ultrasound was especially inaccurate for small lesions.

There was no correlation between the size of the lesion and either the pre-operative pain score or the change in pain score following surgery.

Reliance on single modality imaging would have led to inaccurate diagnosis in 18 cases and would have only benefited one patient. Even imaging with both modalities failed to meet the predictive values attained by clinical assessment.

There is no requirement for ultrasound or MRI in patients who are thought to have a Morton's neuroma. Small lesions, < 6 mm in size, are equally able to cause symptoms as larger lesions. Neurectomy provides an excellent clinical outcome in most cases.

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For most patients with symptomatic Morton's neuromas, the decision to operate has traditionally been based on clinical assessment. Many authors consider the use of pre-operative MRI and ultrasound as useful adjuncts for the diagnosis and

localisation of the neuromas.¹⁻¹² Accurate pre-operative assessment could perhaps enhance the outcome of surgical treatment and imaging could decrease the need to explore adjacent web spaces and avoid vascular compromise of a digit.

Some consider imaging necessary only for those cases where it is difficult to be sure of the site of the lesion or where the history is atypical. Others have preferred imaging to clinical judgment, and recommended its routine use before surgery.^{2,11} This is a waste of resources and sets a dangerous medico-legal precedent. Some have not found ultrasound or MRI to be reliable,^{9,12} especially for smaller lesions.² The prevalence of lesions resembling Morton's neuromas in asymptomatic patients has led some to the conclusion that the imaging modalities have no place in the pre-operative assessment of patients.^{9,12,13}

Several authors have reported the sensitivity and specificity of ultrasound^{1,4,6,7,10,12} and MRI^{3,5,6} with subsequent clinical and histological findings, but most are retrospective and few correlate their findings with the clinical outcome. Whilst MRI is less operator-dependent than ultrasound,^{2,3} there is little direct comparison of these techniques.

One study has compared ultrasound with MRI in patients with a suspected Morton's neuroma.¹² The authors found poor sensitivity for both modalities and found them "of little or no value", but they only considered nine patients from a poorly-defined subgroup and no clinical observations were reported. This study had sensitivity and specificity figures which seem incompatible with current literature. However, in their conclusion, it was suggested that a larger study using more powerful MRI and ultrasound equipment combined with surgical and histological confirmation was warranted. The current study was undertaken to assess these diagnostic techniques using a larger group of cases.

In addition, some authors maintain that lesions found to be small in diameter, <6 mm, on imaging do not cause symptoms.^{4,13} However, if the assessment of size on imaging was inaccurate then this statement would have no basis.

This is the first prospective study to compare ultrasound and MRI findings in the same cohort of patients in order to determine their value in helping to make an accurate diagnosis. The correlation of clinical outcome with radiological, surgical and histological findings is reported. The subgroup of lesions <6 mm in diameter is also considered.

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Patients and Methods

All patients with a clinical diagnosis of a Morton's neuroma who were referred to the senior author (TSS) and who were thought to require surgery had pre-operative ultrasonography and MRI on, or immediately before the day of operation. The clinical criteria for recommending surgical treatment were clearly subjective, but abnormal pain in the second or third web spaces with a palpable 'Mulder's click' and/or a palpable lesion with no other obvious cause of pain, such as metatarsophalangeal joint instability or abnormalities on radiographs, led to a clinical diagnosis of a neuroma.

Details of patient history and results of clinical examination including a visual analogue pain score were recorded on a standard proforma. All patients were assessed at six, 12 and 26 weeks and were sent a final questionnaire at six to 24 months post-operatively.

Patients with recurrent Morton's neuromas were excluded from the trial. The trial consisted of 31 patients, three of whom had suspected bilateral neuromas, but only 25 patients with 29 lesions were available for full final assessment. Of the final 25 patients, 20 were women and five were men, with a mean age of 52 years (34 to 74). The right foot was affected in 15 cases, the left in seven and both feet in three. One patient was found to have neuromas in both the second and third web space of the same foot.

MRI was performed to a set protocol on a 1.5 Tesla machine (GE Medical Systems, Waukesha, Wisconsin), with axial T2 sequences and axial/coronal T1 sequences. All were reported by the same radiologist, a specialist in musculoskeletal MRI.

Another musculoskeletal radiologist carried out the ultrasound using a 12 MHz linear transducer along the sagittal and axial planes. Most of the ultrasound was performed on the dorsal surface of the foot, balloting the web space from below if necessary, but a few of the lesions were more clearly seen from the plantar aspect.

The radiologists reporting the MRI and ultrasound were blinded as to the findings of the other imaging and the senior surgeon (TSS) was also blinded as to the pre-operative test results, but the assistant knew the result in case of a negative exploration.

Both the second and third web spaces were explored in every patient through a single dorsal incision with division of the intermetatarsal ligament and neurectomy of lesions suspected to be Morton's neuromas. Patients were mobilised immediately in a canvas/wooden-soled shoe.

The presence, site and size of the lesions which were excised were recorded and compared with the pre-operative imaging findings. The clinical outcome was scored according to Biasca et al¹¹ and Kitaoka et al.¹⁴

Statistical methods. Descriptive statistics (SAS 8.02; SAS Institute Inc, Cary, North Carolina) were obtained for ultrasound, MRI and for the size of the Morton's neuroma on histology (Table I).

Table I. Descriptive statistics

	Ultrasound	MRI	Histological examination
Mean (mm)	6.52	7.38	8
Standard deviation (mm)	4.93	4.55	3.37
Maximum (mm)	17	17	15
Minimum (mm)	0	0	0
Number of lesions	29	29	29
Number of lesions (< 6 mm)	11	8	6

Table II. The pre-operative clinical features

Clinical signs	Percentage of patients
Plantar pain	100
Pain increased on walking	96
Pain worse in shoes	76
Pain relieved by rest	84
Nature of pain	
Burning	32
Ache	28
Sharp	24
Combination	16
Paraesthesia	68
Mulder's click	84
Radiation up leg	24
Other nerve entrapments	4

Estimates of sensitivity, specificity and positive and negative predictive value were made. Confidence intervals for these statistics were assessed by the efficient-score method incorporating a continuity correction.¹⁵ Consistent biases in the detection of a Morton's neuroma before surgery were assessed using paired Student's *t*-tests [SAS 8.02] with a null hypothesis of no difference among means. The Bland-Altman procedure¹⁶ was used to analyse both the accuracy (i.e., bias) and the amount of variation or precision between the individual test methods (ultrasound and MRI) and histological examination.

Results

A total of 25 patients, with 29 lesions, completed the trial protocol and 28 were found on histological examination to be neuromas, 22 in the third web space and seven in the second web space. The remaining lesion was a rheumatoid bursa in the third web space.

The lesions ranged in size at histological and surgical measurement from 3 to 15 mm and symptoms had been present for a mean of eight months (four months to 20 years). The pre-operative clinical features are shown in Table II.

The diagnosis and site of all but two lesions was correctly identified clinically. In one, the lesion was found to be a rheumatoid bursa in a patient without a previous history of rheumatoid disease. In the other, a lesion unsuspected clinically was found in the third web space, although on clinical grounds, it was thought that only the second web space was involved.

Table III. The MRI findings of lesions correctly identified as Morton's neuromas

Lesion	Findings on T1	Findings on T2	Other comments
1	Intermediate	Low/intermediate	Adjacent cystic area also
2	Intermediate	Intermediate	
3	Low	High	Cystic area in lesion
4	Low	Increased	
5	Low	Increased	
6	Low/intermediate	Intermediate/high	Fluid adjacent lesion also
7	Intermediate	Increased	
8	Decreased signal	Intermediate and high	
9	Low/intermediate	Intermediate	
10	Low/intermediate	Mild increased	
11	Low	High	
12	Low	High	
13	Intermediate	Low with fluid	
14	Intermediate	Increased	T2 increased with contrast
15	Low/intermediate	Increased	
16	Low/intermediate	Intermediate/high	
17	Low	Low	Low on Stir T2
18	Low	No T2 sequence done	High on T1 Stir
19	Increased	Increased	
20	Increased	Increased	
21	Low/intermediate	Intermediate	
22	Intermediate	Increased	
23	Low	Intermediate	Some fluid adjacent
24	Low/intermediate	No comment	

Table IV. Clinical outcome from neurectomy

	Respondents (%)
I am essentially pain free; I can wear almost any shoes and do any activities I like	58
Mild/moderate pain, moderate restrictions with my footwear and activities	42
The operation has made no difference to my pain or has even made it worse	0
I have major restrictions with my footwear and activities	
Completely satisfied	63
Satisfied with a few reservations	26
Satisfied with some major reservations	11
Dissatisfied	0
I wish I'd never had surgery	0

Pre-operative ultrasound missed six lesions, incorrectly suggested the presence of three in adjacent web spaces, but correctly identified the rheumatoid bursa as not being a neuroma. All but one lesion were hypoechoic, with the remaining lesion having a solid cystic component. Ultrasound correctly identified the size of the neuroma, within 2 mm of the histological and surgical size in 13 cases, overestimated the size in three cases and underestimated it in six. All but two of the six lesions missed by ultrasound were <6 mm in diameter. Of the six lesions <6 mm at histology, ultrasound identified three (Table I).

MRI missed four lesions, incorrectly suggested the presence of five in adjacent web spaces but correctly identified the rheumatoid bursa. MRI also pre-operatively identified a second lesion in the third web space when clinical suspicion had only suspected a lesion in the second. The features from an MR scan of the lesions correctly identified as being Morton's neuromas are shown in Table III. MRI correctly identified the size of the lesion, within 2 mm of clinical/histological size, in 11 cases, overestimated the size in ten and underestimated it in three. Contrast was necessary in

only one patient and two others had spin sequences in addition to axial T2 and axial/coronal T1 scans.

One patient had a post-operative deep venous thrombosis and three had post-operative wound infections treated with oral antibiotics.

Most patients had marked clinical improvement following surgery (Table IV) and this was significant at the 5% level. Most reported that they felt cured by the post-operative visit at six weeks despite some residual discomfort.

Use of imaging to predict the presence of a Morton's neuroma. Clinical pre-operative examination accurately identified the presence of a neuroma. There was a significant difference between the accuracy of diagnosis by clinical assessment, ultrasound and MRI. The sensitivities of ultrasound and MRI are significantly < 1 (Table V), while the sensitivity of surgical assessment did not differ significantly from 1. The specificities were high for MRI and ultrasound while difficult to assess for surgical assessment. Positive-predictive values were high for all methods. Negative-predictive values were difficult to assess as there was only one negative histology. The sensitivity of ultrasound

Table V. Sensitivity, specificity, positive and negative predictive values for different methods of predicting the presence of Morton's neuroma (assessed by histological examination)

	Ultrasound	MRI	Surgical assessment
Sensitivity	0.79 (0.59, 0.91)*	0.86 (0.64, 0.95)	1.00 (0.85, 1.00)
Specificity	1.00 (0.055, 1.00)	1.00 (0.05, 1.00)	0.00 (0.00, 0.95)
Positive predictive value (true-positive)	1.00 (0.82, 1.00)	1.00 (0.82, 1.00)	0.97 (0.80, 1.00)
Positive predictive value (true-negative)	0.14 (0.01, 0.58)	0.20 (0.01, 0.70)	n/a [†]

*lower 95% confidence limit, upper 95% confidence limit

[†]histological examination was done on all surgical specimens independent of image analysis**Table VI.** Sensitivity, specificity, positive and negative values for different methods of predicting the presence of Morton's neuroma (assessed by histological examination) for lesions of < 6 mm

	Ultrasound	MRI	Surgical assessment
Sensitivity	0.50 (0.14, 0.86)*	0.83 (0.36, 0.99)	1.00 (0.52, 1.00)
Specificity	1.00 (0.05, 1.00)	1.00 (0.05, 1.00)	0.00 (0.00, 0.95)
Positive predictive value (true-positive)	1.00 (0.31, 1.00)	1.00 (0.46, 1.00)	0.86 (0.42, 0.99)
Positive predictive value (true-negative)	0.25 (0.01, 0.78)	0.50 (0.03, 0.97)	n/a [†]

*lower 95% confidence limit, upper 95% confidence limit

[†]histological examination was done on all surgical specimens independent of image analysis**Table VII.** Bias assessed by paired *t*-test

	Histological-Ultrasound	Histological-MRI	MRI-Ultrasound
t-statistic (T)	2.235	0.856	0.857
Critical t (two-tail) (alpha = 0.05)	2.048	2.048	2.048
Probability (T <= t)	0.0335*	0.399	0.398

*significant at 5% level

Table VIII. Bland-Altman agreement statistics for paired samples

	Ultrasound-Histological	MRI-Histological
Mean difference	1.48 (0.15, 2.81)*	0.62 (-0.83, 2.07)
Upper limit of agreement (95% confidence)	8.63 (6.33, 10.93)	8.43 (5.91, 10.94)
Lower limit of agreement (95% confidence)	-5.66 (-7.96, -3.35)	-7.19 (-9.70, -4.70)*

*lower confidence limit, upper confidence limit at 95% levels

decreased to 50% for lesions <6 mm on histology (Table VI). The decrease in sensitivity of ultrasound was greater than the decrease of MRI for small lesions.

Ultrasound ($p = 0.034$) underestimated the mean size of the lesion, which, when assessed by MRI, did not differ significantly from the mean histological size (Table VII).

The histological size of the lesion could be predicted either by ultrasound or MRI; thus there was a wide range of agreement in relation to the mean histological size (8 mm) (Table VIII). Measurement by ultrasound was 5.7 mm less than or 8.6 mm more than the size of the lesion. Measurement by MRI was 7.2 mm less than or 8.4 mm more than the size of the lesion. It is highly probable that small lesions

will remain undetected by both screening procedures, which tend to underestimate the size of smaller lesions and overestimate that of larger ones. While the mean size of neuromas on MRI does not differ significantly from the mean size on histology, individual lesions vary considerably. MRI is sufficiently sensitive to detect the presence of a lesion but it cannot accurately predict the size. Ultrasound cannot reliably predict the size of individual lesions.

Discussion

Morton's metatarsalgia was first described by Durlacher in 1845.¹⁷ Morton himself described the syndrome some 31 years later when describing a lesion between the third and fourth metatarsals.¹⁸ Most commonly affecting the third web space in middle-aged females, characteristic symptoms include burning, numbness, discomfort with shoe wear and the feeling of a pebble under the metatarsal region. The reported positive-predictive values of various symptoms and signs, such as the Mulder's click, have been reported and vary enormously.^{3,6-8,11,12,19} The differential diagnosis includes inflammatory, neurological and biomechanical causes, stress fractures, Freiberg's disease, infection and

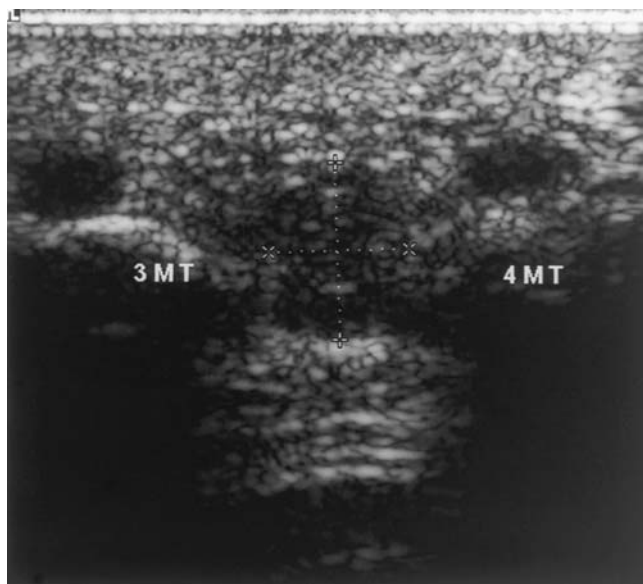


Fig. 1

An ultrasound showing the hypoechoic lesion between the 3rd and 4th metatarsal (MT) heads.

tumours. The diagnosis is based on clinical assessment, with radiographic and serological exclusion of other lesions. The pathology causing the symptoms is not clear. Betts proposed that the communicating branch to the interdigital nerve of the third web space from the fourth tethers the nerve, making it vulnerable to repeated trauma at the edge of the intermetatarsal ligament.²⁰ Nissen, however, thought the pathology to be vascular leading to neurofibrosis and others have suggested a compression phenomenon in the tunnel formed by the superficial and deep transverse intermetatarsal ligaments.^{21,22} Bossley and Cairney²³ suggested that the neuroma is caused by compression of the nerve due to swelling of the intermetatarsal bursa. The presence of Renault bodies, indicating neural compression, in retrieved pathological specimens supports a compressive theory, as similar lesions are seen in other peripheral compression neuropathies. However, not all nerves which have been removed from patients with reported cure show these features and the vascular theory would seem to explain the presence of symptoms in nerves with a normal diameter. This has implications for the value of imaging modalities which identify a neuroma by a change in the width of the nerve. If we accept that a proportion of nerve lesions causing symptoms are of normal size, then no imaging test can claim 100% sensitivity.

Many different techniques have been used to aid the clinical diagnosis of a neuroma; CT scanning, electrophysiology and the injection of local anaesthetic^{19,25} have been reported as useful for confirmation of the diagnosis, but may involve radiation, cumbersome techniques and have doubtful specificity. MRI and ultrasound are the modalities most

widely reported. Ultrasound has generally good specificity and sensitivity (0.65 to 0.98) for Morton's neuromas,^{1,2,4,6,7,10} although some authors doubt its use as the distribution of lesions has been reported as the same in both symptomatic and asymptomatic individuals.⁴ Scanning in the sagittal plane has been shown to eliminate some of the false positive results which were caused by incorrect identification of the distal end of the interossei as neuromas.⁷ The characteristics of lesions on ultrasound change with time, with younger lesions showing hypoechoicity, and older lesions hyperechoicity.⁸

Ultrasound has been shown to be user dependent and in several reports comparing ultrasound with surgical and histological findings, it was shown to overestimate the size of lesions and this was thought to be due to the signal arising from surrounding mucoid degeneration and intermetatarsal bursae (Fig. 1).^{7,10}

While Shapiro and Shapiro¹ claimed 98% accuracy for pre-operative ultrasound, they reported no clinical outcomes and did not mention the size of the lesions which were detected and removed. Similarly Jones et al¹⁰ claimed 95% accuracy for ultrasound but their patients only had operations if a lesion was seen on ultrasound so it is impossible to gauge the number of false negative results.¹⁰ Volpe et al⁶ found ultrasound to be 80% accurate, with all the false negatives being for neuromas <6 mm in size at surgery.⁶ Redd et al⁴ used ultrasound to show that neuromas were prevalent in the same anatomical patterns in both symptomatic and asymptomatic individuals, but only lesions of >5 mm in size caused symptoms. Resch et al¹² found that ultrasound was of no use in detecting Morton's neuromas.

Many authors have considered MR scanning as a more useful test (Figs 2a and 2b). In 1991 Erickson et al³ using the MRI characteristics of neuromas described by Sartoris et al⁵ in 1989 showed that MRI was an "accurate and operator-independent modality", despite a 16% false positive rate for detecting Morton's neuromas in six patients. Erickson et al used an extremity MRI coil,^{3,24} whereas subsequent reports have used more traditional body scanners. Terk et al⁹ found that a combination of fat suppression and contrast enhancement provided reliable high-contrast images, the T1-weighted image being the most useful. In an MRI study, Zanetti et al¹³ showed a prevalence of Morton's neuromas of 30% in 70 asymptomatic individuals and compared these results with a group of symptomatic patients reviewed retrospectively following excision and histological confirmation. They found that a neuroma size of 5 mm was significantly associated with symptoms ($p = 0.0075$). They also defined three MR criteria for the diagnosis of Morton's neuroma; it should be centred in the region of the neurovascular bundle within the intermetatarsal space and on the plantar side of the transverse ligament, it should be well demarcated, and have a characteristic signal intensity (isointense relative to muscle on T1-weighted images and homogeneously or inhomogeneously hypointense relative to fat tissue on T2-weighted images). In another MR study

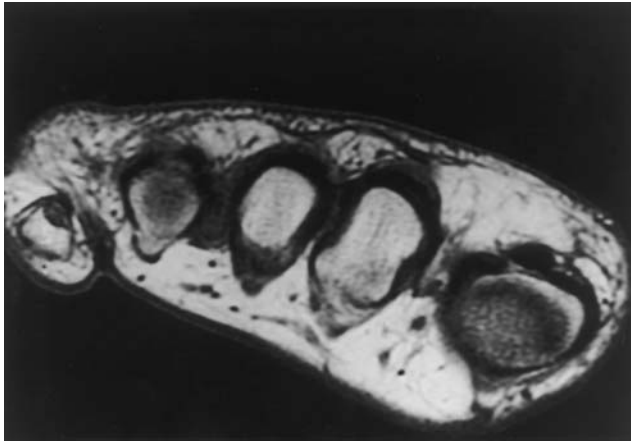


Fig. 2a

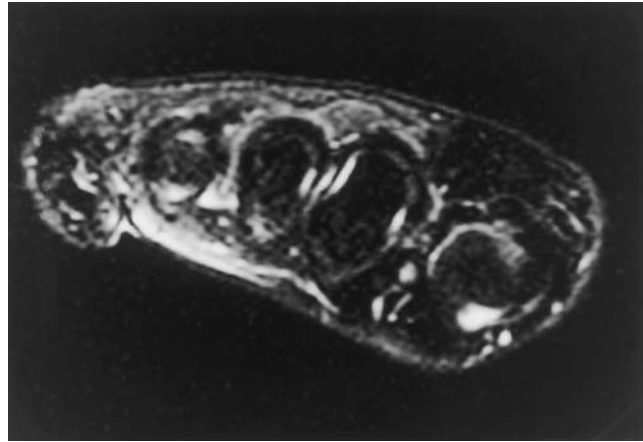


Fig. 2b

(a) A T1-weighted MR scan showing the Morton's neuroma between the 3rd and 4th metatarsal heads and (b) A T2-weighted MR scan showing the typical characteristics of a Morton's neuroma between the 3rd and 4th metatarsal heads but with some surrounding fluid (high signal).

Zanetti et al² studied scans of 18 intermetatarsal spaces in 16 patients with 15 surgically proven neuromas. They found 13 true-positive, two false-negative, three true-negative, and no false-positive MR diagnoses and concluded that a limited examination using axial T1-weighted spin-echo images was adequate with additional sequences being recommended only for differential diagnoses. Resch et al¹² similarly found a 40% false-positive rate with gadolinium contrast.

Imaging characteristics. Hypoechoicity was a consistent finding on ultrasound and we found no cases with hyperechoicity as has been previously described in older lesions. Some of the MRI features on T2 sequences previously attributed to Morton's neuromas were not consistently found in our study. T1 and T2 sequences were adequate for diagnosis in all but three cases in which a spin sequence or contrast were used. Low or intermediate signal on T1-weighted MR images isointense with muscle was a consistent feature, but the T2 findings were more varied and followed no obvious pattern (Table III). Our radiologist felt that the most consist-

ent feature of a Morton's neuroma is on T1-weighted images, looking for a solid lesion isointense to muscle and surrounded by a small halo of fat. T2 images may help in excluding lesions which are cystic, such as ganglions and bursae. Contrast would only be necessary to exclude neurofibromas that show high signal on T2.

While the frequency of clinical features elicited can be seen in Table I, no particular feature would be adequate to confirm the diagnosis. The reproduction of symptoms for the patient and a crackling sensation felt by the examiner while the metatarsals are compressed was felt to be the most accurate clinical predictor of a neuroma.

It would be impossible to gain a true picture of the false-negative rate of clinical acumen without operating on all patients with metatarsalgia of undiagnosed aetiology. Only one patient was found to have a missed Morton's neuroma at surgery indicating the accuracy of clinical assessment. The false-positive rates for ultrasound and MRI were 11% and 20%, although this only includes the adjacent web space to that explored at surgery. We found no lesions on

Table IX. The correlations between modalities in Morton's neuromas imaged prior to surgical excision

	Size on ultrasound (mm)	Size on MRI (mm)	Size at histology/surgery	Pain score pre-operatively	Pain score post-operatively	Change in pain
Size on US (mm)	1					
Size on MRI (mm)	0.35 (-0.02, 0.62)	1				
Size at histology/surgery	0.69 (0.43, 0.85)	0.55 (0.22, 0.77)	1			
Pain score pre-op	0.23 (-0.16, 0.56)	0.19 (-0.20, 0.53)	0.20 (-0.19, 0.53)	1		
Pain score post-op	0.08 (-0.30, 0.44)	0.23 (-0.16, 0.56)	0.08 (-0.30, 0.44)	-0.17 (-0.51, 0.21)	1	
Change in pain score	0.13 (-0.26, 0.48)	0.02 (-0.36, 0.39)	0.10 (-0.28, 0.46)	0.84 (0.68, 0.92)	-0.67 (-0.83, 0.39)	1

*Correlation shown in **bold type** (lower confidence limit, upper confidence limit at 95% level shown beneath)

MRI or ultrasound in either the first or fourth web space, but these were not explored surgically.

Size of lesion and clinical effect. The size of lesion, whether measured clinically, with ultrasound or with MRI showed no correlation with the visual analogue score of pain, nor with the change in pain score following surgery (Table IX). The effect of size of the nerve on symptoms has been studied; some authors have found a strong correlation between lesions >5 mm in size^{2,4} and the presence of symptoms and excision of larger lesions has been found to offer higher cure rates than removal of smaller lesions. Others doubt that lesions <5 mm in size can cause symptoms and MR studies in asymptomatic patients have found the presence of lesions which resemble neuromas in up to 30% of patients.¹³ Biasca et al¹¹ reported that lesions <5 mm in size but producing symptoms consistent with metatarsalgia were treated successfully with neurolysis and division of the intermetatarsal ligament, whereas larger lesions were treated with excision.

We have treated all lesions, regardless of size by neurectomy. Histology has been compatible with Morton's neuromas in all but one specimen and in this one case, the incorrect diagnosis was obvious at the time of surgery. All but one of our patients had significant improvement in symptoms and there was no correlation between the size of lesion and either the presenting symptoms or the change in symptoms following surgery. We do not agree that only lesions >5 mm in size cause symptoms.

The clinical outcome was excellent or good in 89% of patients but 11% had major reservations with the result of surgery (Table IV).

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