Ultrasound Evaluation of Morton Neuroma Before and After Laser Therapy

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OBJECTIVE. The objective of our study was to retrospectively assess for differences in imaging appearances of Morton neuromas before and after laser therapy using diagnostic ultrasound (US).

MATERIALS AND METHODS. A retrospective review was performed to identify patients who underwent US imaging to evaluate for Morton neuroma during the study period (June 1, 2013–July 1, 2014); of the 42 patients identified, 21 underwent US evaluations before and after laser therapy. US reports and images were reviewed and correlated with clinical history. The final study group consisted of 21 patients who had a total of 31 Morton neuromas evaluated using US after treatment. A retrospective review was then performed to characterize the appearances of these lesions before and after therapy followed by an analysis of variables.

RESULTS. Retrospective US review of 31 pretreatment Morton neuromas showed fusiform, heterogeneously hypoechoic masses with well-defined borders in most cases and that pain was reported when transducer pressure was applied in 97% (30/31) of cases. After treatment, lesions showed ill-defined borders (23/31), and pain with application of transducer pressure was either significantly decreased or absent (29/31); these findings were concordant with the clinical findings. Both of these characteristics were statistically significant (p < 0.0001). In addition, more Morton neuromas occurred in the second intermetatarsal space than in the third intermetatarsal space (p < 0.0001).

CONCLUSION. US may be used to identify posttreatment changes after laser therapy of Morton neuromas. Posttreatment changes include ill-defined borders and less pain or the absence of pain with the application of transducer pressure. These criteria may be applied in future clinical studies evaluating the efficacy of laser therapy for Morton neuroma.



orton neuroma results from the nonneoplastic fusiform enlargement of the plantar digital nerve and is not a true neuroma; rather,

Morton neuroma consists of edema, perineural fibrosis, axonal degeneration, and local vascular proliferation at the level of the metatarsal heads just plantar to the intermetatarsal ligament [1, 2]. This lesion is a common cause of forefoot pain, which manifests as metatarsalgia. Pain radiates from the midfoot to the toes and may be associated with the Tinel sign (i.e., light percussion over the nerve elicits a sensation of tingling or "pins and needles" in the distribution of the nerve) and the Mulder sign (a palpable click elicited by squeezing the metatarsal heads together with one hand while concomitantly putting pressure on the interdigital space with the other hand) [3]. Morton neuromas may be multiple and bilateral and, according to the literature, occur most commonly at the third intermetatarsal space [4].

Although clinical examination remains the diagnostic reference standard for Morton neuroma [5], evaluations with ultrasound (US) and MRI have been shown to be useful for the diagnosis and preoperative localization of Morton neuroma, particularly when lesions are multiple or the presentation is atypical [2, 6]. Previous studies have found that large Morton neuromas (> 5 mm) are more likely to be symptomatic and are more commonly treated surgically than small Morton neuromas [7].

A variety of therapeutic approaches are available for the treatment of symptomatic Morton neuromas beginning with conservative measures, such as footwear modification and steroid injections, followed by more invasive methods, including ultrasound-guided cryoneurolysis, radiofrequency or alcohol ablation with progression to digital neurecto-

380 AJR:208, February 2017

Ultrasound of Morton Neuroma

my, percutaneous osteotomy, and intermetatarsal ligament release for refractory lesions [5, 8–11]. We have seen increasing US referrals for pretreatment diagnosis and posttreatment follow-up of Morton neuromas before and after high-intensity laser therapy (HILT). HILT has not been previously reported, to our knowledge, as a treatment method for Morton neuroma in the English-language literature. Currently, HILT has been approved by the U.S. Food and Drug Administration for the treatment of various skin lesions, hair removal, tattoo removal, and onychomycosis but not for the treatment of Morton neuroma.

The purpose of our study was to retrospectively determine the differences in US appearances of Morton neuromas before and after HILT.

Materials and Methods

Institutional review board approval was obtained, and informed consent was waived. Musculoskeletal US case logs from June 1, 2013, through July 1, 2014, were searched to identify patients who underwent US for evaluation of Morton neuroma. Medical records, including other correlative imaging findings and clinical history, were reviewed. The initial review of musculoskeletal US case logs identified 42 patients who underwent forefoot US for suspected Morton neuroma and 21 patients who underwent US evaluations before and after HILT.

The inclusion criteria for the HILT procedure were the presence of symptomatic Morton neuroma that had been confirmed with a baseline diagnostic US examination. Conservative treatment of Morton neuroma in these patients had failed. The exclusion criteria were prior surgery for Morton neuroma or

the presence of peripheral or diabetic neuropathy. A follow-up diagnostic US examination was performed to evaluate for imaging changes seen after laser treatment. The decision to use HILT to treat symptomatic Morton neuromas in our patients was based on the safety, effectiveness, and clinical applications of a neodymium:yttrium-aluminumgarnet (Nd:YAG) laser (GenesisPlus, Cutera).

In our patients, the HILT treatment of Morton neuroma was performed as a series of 10 treatments once a week in an office setting after informed consent was obtained. The procedures were performed in a designated laser treatment room. Protective glasses were worn by the treating physician. The lesions were localized under US guidance. The procedures were performed without anesthesia. A topical compounded medication containing verapamil 15%, pentoxifylline

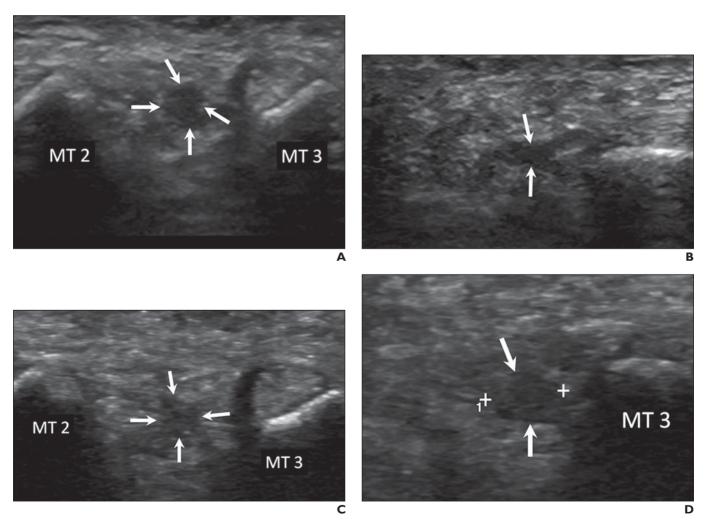


Fig. 1—75-year-old man with metatarsalgia at second interspace who underwent high-intensity laser therapy (HILT) for treatment of Morton neuroma.

A and B, Gray-scale short-axis (transverse) (A) and long-axis (B) ultrasound (US) images obtained before HILT show round hypoechoic lesion between second (MT 2) and third (MT 3) metatarsal heads with well-defined borders (arrows). In real-time ultrasound examination, lesion was seen in continuity with digital plantar nerve.

C and D, Gray-scale transverse (C) and long-axis (D) US images obtained after HILT show round hypoechoic lesion in similar position with ill-defined borders (arrows) relative to adjacent soft tissues. In D, cursors and 1 indicate calipers for measurement of lesion. MT 2 = second metatarsal head, MT 3 = third metatarsal head.

AJR:208, February 2017 381

Gimber et al.

3%, and tranilast 1% was applied directly to the area demarcated at the location of the neuroma at the plantar aspect of the foot. HILT was performed using a Nd:YAG laser with the following parameters: fluence, 15 J/cm²; pulse width, 0.3 ms; and repetition rate, 7 Hz. Laser energy (total = 1000 pulses) was directed at the lesion site. The laser treatment was briefly interrupted to allow gentle massage of the area and was then immediately resumed until a total of 1000 pulses had been delivered to the site. During the HILT treatment, all patients experienced little to no discomfort throughout the entire procedure. The patients were allowed to return to normal shoe gear and to resume normal activities as tolerable. Tight shoes (high heels) are not allowed during the course of the 10-week treatment.

US examinations were performed as part of routine clinical practice at our institution on a US machine with a high-resolution 8-18-MHz multifrequency linear "hockey stick" transducer (Logiq E9, GE Healthcare) by a musculoskeletal US technologist. US examinations performed after HILT were performed by a fellowship-trained musculoskeletal radiologist. US examinations were performed with the patient supine, and evaluations of all intermetatarsal spaces were performed using a plantar approach as described by Quinn and collaborators [2]. We also examined the adjacent plantar plates and flexor tendons to exclude other abnormalities that could cause pain in the same region. Equal pressure was applied on the dorsal aspect of the imaged intermetatarsal head space from the sonographer's nonimaging finger to assist in visualization by splaying the metatarsals. Imaging from the dorsal aspect of the intermetatarsal head spaces was not performed. Liberal sonographic transmission gel was used in place of a standoff pad. Dynamic US imaging was performed to assess for the Mulder sign and to evaluate for reproducible pain during application of transducer pressure. Gray-scale images were acquired in the transverse (short axis) and longitudinal (long axis) planes relative to the metatarsal shafts, perpendicular to and in the plane of the plantar digital nerve, respectively, with routine use of color and power Doppler imaging. Static images and cine clips were stored on the department's PACS.

A retrospective consensus review of the US images of the final study group was then performed by two fellowship-trained musculoskeletal radiologists (3 and 20 years of experience). Static and cine images were reviewed, and each pretreatment Morton neuroma was evaluated for size, location, echogenicity, echotexture, overall shape (round or fusiform), borders (well defined or ill defined), hyperemia, presence of bursa, presence of pain with transducer pressure, and presence of Mulder sign. Each posttreatment Morton neuroma was also reviewed with attention to these same parameters. These data were then evaluated to determine whether any of the US variables permitted differentiation of pretreatment Morton neuroma from posttreatment Morton neuroma. Chi-square tests were used for all categoric variables.

Results

The final study group of 21 subjects consisted of 81% women (17/21) and 19% men (4/21) with an average age of 62.5 years (range, 29-85 years). The right foot was involved in 38% (8/21), the left foot in 48% (10/21), and both feet in 14% (3/21). A total of 31 Morton neuromas were treated, including

12 left foot lesions and 19 right foot lesions. Of the treated lesions, 77% (24/31) were located in the second intermetatarsal space and the remaining 23% (7/31) were located in the third intermetatarsal space, which was a statistically significant difference (p < 0.0001).

Retrospective review of the initial US studies of Morton neuromas (Table 1) showed the average lesion size before treatment was 4.1 mm (range, 2.0-12.0 mm). All lesions were heterogeneously hypoechoic with fusiform shape in 97% (30/31) (Figs. 1 and 2). There was associated pain with transducer pressure in 97% of lesions (30/31). The lesion borders were well defined in 87% of cases and ill defined in the remaining 13%. There was

TABLE I: Ultrasound Characteristics of Morton Neuromas Before and After High-Intensity Laser Therapy (HILT)

Ultrasound Characteristics	Before HILT	After HILT
Lesion size (mm)		
Average	4.1	2.3
Range	2.0-12.0	0.8-4.5
Lesion size after HILT ^a		
Stable		48 (14/29)
Decreased		59 (17/29)
Pain		
Moderate to severe	97 (30/31)	6 (2/31)
Mild	0 (0/31)	13 (4/31)
Absent	3 (1/31)	81 (25/31)
Echogenicity		
Hypoechoic	100 (31/31)	100 (29/29)
Echotexture		
Heterogeneous	100 (31/31)	100 (29/29)
Shape		
Round	3 (1/31)	14 (4/29)
Fusiform	97 (30/31)	86 (25/29)
Borders		
Well defined	87 (27/31)	28 (8/29)
III defined	13 (4/31)	72 (21/29)
Hyperemia		
Absent	0 (0/31)	0 (0/31)
Mulder sign		
Present	3 (1/31)	0 (0/29)
Absent	97 (30/31)	100 (29/29)
Associated bursa		
Present	10 (3/31)	0 (0/31)
Absent	90 (28/31)	100 (31/31)

Note—All results except size data are presented as % (no. of cases / total no. of cases).

^aTwo lesions were not seen on ultrasound after HILT

382 AJR:208, February 2017

Ultrasound of Morton Neuroma

no evidence of lesion hyperemia on color or power Doppler imaging. A positive Mulder sign was present in only 3% (1/31) with an associated intermetatarsal bursa in 10% (3/31) (Figs. 2A and 2B). The average time from initial US to treatment completion was 103 days (range, 41–243 days).

The average time from treatment to follow-up US was 51 days (range, 13–116 days). Review of posttreatment images revealed persistently visible lesions in 94% (29/31) and nonvisualization in 6% (2/31). Lesion size decreased in 59% (17/29) and remained stable in 48% (14/29). All visualized posttreatment lesions remained heterogeneously hypoechoic; 86% of posttreatment lesions were fusiform and 14% were round. In addition, 72% of lesions had ill-defined borders

TABLE 2: Analysis of Ultrasound (US) Findings Before and After High-Intensity Laser Therapy of Morton Neuroma

	Statistical Results	
US Findings	χ^2	р
Change in lesion size	1.03	
Pain with transducer pressure	50.66	< 0.0001a
Echogenicity	0	
Echotexture	0	
Shape	4.30	< 0.05ª
Borders	24.09	< 0.0001a
Hyperemia	0	
Mulder sign	1.03	
Associated bursa	5.16	< 0.05a

^aStatistically significant.

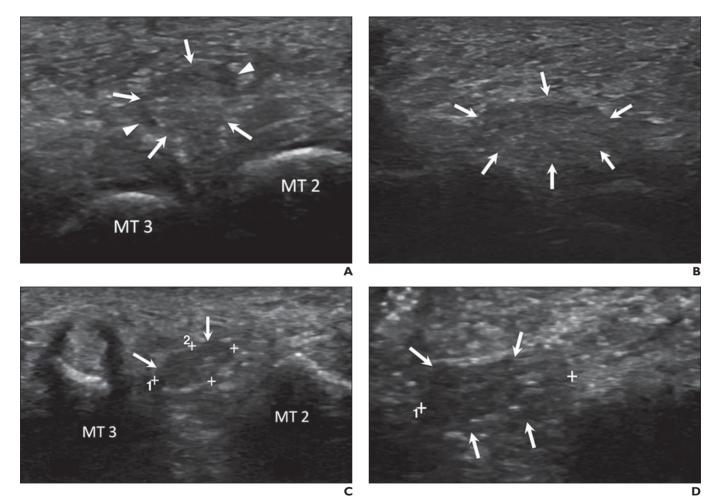


Fig. 2—68-year-old woman with right foot metatarsalgia at second interspace who underwent high-intensity laser therapy (HILT) for treatment of Morton neuroma. A and B, Gray-scale short-axis (transverse) (A) and long-axis (B) ultrasound (US) images obtained before HILT during positive Mulder test show hypoechoic lesion (arrows) arising between second (MT 2) and third (MT 3) metatarsal heads surrounded by hypoechoic bursal fluid (arrowheads, A); these findings are consistent with Morton neuroma and associated bursitis. In real-time US examination, lesion was seen in continuity with digital plantar nerve.

C and D, Gray-scale short-axis transverse (C) and long-axis (D) US images obtained after HILT show smaller hypoechoic lesion in same location (arrows) without surrounding bursal fluid; these findings are consistent with posttreatment changes. On follow-up study, Mulder test was negative. In C, MT 2 indicates second metatarsal head; MT 3, third metatarsal head; cursors and 1 and 2 indicate calipers for measurement of lesion. In D, cursors and 1 indicate calipers for measurement of lesion.

AJR:208, February 2017 383

Gimber et al.

(21/29) (Figs. 1C and 1D), whereas 28% remained well defined (8/29). There was no bursa, Mulder sign, or Doppler signal associated with any of the treated lesions. Pain with transducer pressure resolved in 81% (25/31) of lesions and decreased to mild in 13% (4/31); moderate to severe pain persisted in only 6% (2/31) of lesions. Additionally, all patients who did not have pain with transducer pressure on follow-up US studies reported complete resolution of pain including with weight-bearing and ambulation. Likewise, patients who had decreased or persistent pain with transducer pressure on posttreatment follow-up US studies reported pain with weight-bearing and ambulation.

When comparing the US findings of preand post-HILT lesions (Table 2), there were significant differences (p < 0.05) with regard to the presence of pain and bursa and to lesion borders and shape (Fig. 1). In general, posttreatment lesions were associated with decreased pain and showed ill-defined lesion borders; some posttreatment lesions transitioned from fusiform to round shape, and associated bursa, when present, resolved in some cases (Figs. 2C and 2D).

Aside from mild osteoarthritis at the adjacent metatarsophalangeal joints, no additional findings, including plantar plate injuries or tendon abnormalities, were noted to suggest an alternative cause of metatarsalgia in our patients.

Discussion

US has been identified as the most cost-effective and accurate imaging method for diagnosing Morton neuroma [6, 12]. The results of our retrospective study showed that decreased pain with transducer pressure and ill-defined margins were characteristic US features of most Morton neuromas after HILT.

The diagnosis of metatarsalgia due to Morton neuroma requires the exclusion of alternate diagnoses and accurate localization of the symptomatic plantar digital nerves, which can be confounded by lesion multiplicity and small size. Although a transverse diameter of 5 mm has been established to identify Morton neuromas that are likely symptomatic, Bencardino et al. [13] discovered a significant overlap in the sizes of symptomatic and asymptomatic Morton neuromas on MRI and recommended careful clinical correlation. Mahadevan et al. [14] found no correlation between the size of Morton neuroma on US and positive clinical examination findings except the Mulder sign. US permits dynamic assessment of the lesion and allows inves-

tigation of the pain source, including evaluation for Mulder signal and correlation for pain with applied transducer pressure [12]. Pain with transducer pressure was present in all but one of the lesions identified before treatment; however, the average size of the treated lesions was 4.1 mm, and only one lesion measuring 12.0 mm showed the Mulder sign. Real-time US examination allows the effective identification of smaller symptomatic Morton neuromas that may benefit from treatment. Real-time US examination may be particularly useful in identifying symptomatic lesions that are too small to necessitate aggressive operative intervention but that may benefit from a less invasive treatment such as HILT. In all treated lesions, no alternative cause of metatarsalgia was identified on US, including tendon abnormalities and plantar plate tears.

Although it has been theorized that a thicker third intermetatarsal nerve formed by the medial and lateral plantar nerves leads to more frequent entrapment and purportedly results in most neuromas occurring in the third intermetatarsal space, other studies have found that other intermetatarsal spaces may be involved, including the second intermetatarsal space [13, 15, 16], which was the most common site in our study.

After diagnosis and conservative measures, many Morton neuromas are treated by excision of the plantar digital nerve, often through a dorsal approach; however, up to 20-30% of these patients experience recurrent symptoms [17, 18]. Surgical failures have been attributed to recurrent neuroma formation, symptomatic stump neuroma, scar tissue, or inadequate resection [10]. Postsurgical MRI for recurrent metatarsalgia can reveal neuromalike fibrosis and an increased prevalence of intermetatarsal bursitis in symptomatic patients [19]. In a study of 58 consecutive patients undergoing MRI after neuroma resection, prospectively diagnosed recurrent neuromas in seven patients were found to be fibrotic scar without nerve tissue [20]. To date, no studies have detailed the postsurgical US findings after plantar digital nerve excision.

After surgical excision, pain may also persist because of referred symptoms secondary to additional neuromas in adjacent intermetatarsal spaces because most surgeons attempt to avoid excising neuromas in adjacent webspaces [11]. Less invasive methods such as HILT and radiofrequency ablation can be used pre- or postoperatively to address small adjacent neuromas identified on US, thus reducing the risk for recurrent symptoms.

Less invasive nonsurgical approaches attempt to reduce the risk of painful scar formation by minimizing impact on adjacent soft tissues; however, all less invasive treatment methods, including ethanol ablation, radiofrequency ablation, cryoablation, and steroid injection, are believed to alter the relationship of the digital plantar nerve with the surrounding soft tissues. Chuter et al. [11] addressed concerns about perilesion scar formation after radiofrequency ablation impacting future surgical intervention by sharing the surgical observation that posttreatment lesions were firm, scarred, or adherent but remained identifiable without apparent effect on operating time or outcome. After HILT was performed to treat Morton neuroma in our patients, all but two Morton neuromas remained identifiable on US and showed similar echogenicity and echotexture; however, most lesions developed ill-defined borders with the adjacent soft tissues, which is suggestive of scar forming around the treated lesion. There was no evidence of masslike scar surrounding the treated lesions, which could predispose to recurrent impingement or entrapment. Because none of the lesions in our study progressed to excision, the presence of scar tissue around the treated lesion could not be confirmed. Overall, there was no significant interval change in size between the pre- and post-HILT lesions. This finding differs from a report of US findings after ethanol ablation of Morton neuromas that showed a 30% decrease in the size of the neuromas [9]. Although US has also been used to guide cryoneurolysis with a reported 75% positive response rate, no studies have been performed to date to assess the posttreatment US appearance.

The characteristic US appearance of Morton neuroma is a well-defined hypoechoic intermetatarsal mass in continuity with the digital plantar nerve that may be associated with an adjacent intermetatarsal bursa [2]. In our study, a bursa was associated with only three lesions before treatment, and the presence of a bursa may reflect a relationship between the size of the neuroma and the presence of bursal fluid; however, a prior study by Zanetti et al. [21] found no statistically significant correlation between fluid in the intermetatarsal bursa and Morton neuroma in the first and second intermetatarsal spaces on MRI. In our study, all intermetatarsal bursae resolved after treatment, and no lesions showed interval development of bursal fluid. These US findings are similar to previously reported MRI find-

384 AJR:208, February 2017

Ultrasound of Morton Neuroma

ings after Morton neuroma resection in which bursitis was seen in only 9% of asymptomatic patients as opposed to 27% of patients with recurrent symptoms [20]. Dynamic US examination can reveal the presence of the Mulder sign, and the US transducer may be used to elicit pain at the site of the abnormality. Pain was absent or had lessened after HILT in all lesions except two; these findings emphasize the importance of both the posttreatment clinical examination and real-time assessment for pain during US.

There are several limitations to this study. This study was retrospective and included fewer than 50 patients undergoing US evaluation. The retrospective review of the US images was limited to what was initially imaged prospectively and is subject to inter- and intraobserver variability. A selection bias existed because all patients were referred for evaluation of suspected Morton neuroma, and all patients with symptomatic Morton neuromas underwent treatment with HILT. No additional alternative treatment methods were imaged after intervention, and no pathologic correlation was available. In addition, the pre- and post-HILT clinical pain assessments were not standardized. The patients were imaged in a short-term follow-up interval after HILT, and no long-term follow-up imaging was performed. Additionally, there was no control group in our study.

In conclusion, US can be used to identify posttreatment changes after HILT for Morton neuroma. These changes consist of ill-defined lesion borders, a transition in lesion shape from round to fusiform, the resolution of bursa, and resolution or decrease in pain with transducer pressure. The resolved or decreased pain with transducer pressure emphasizes the importance of physical examination findings over imaging features for posttreatment follow-up. Additional prospective studies with long-term imaging follow-up after HILT would be helpful to determine wheth-

er the ill-defined lesion borders are a transient treatment effect and to assess whether symptomatic improvement persists.

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AJR:208, February 2017 385