

SMI – a new technique for the analysis of the microvascular tree in reactive and suspected malignant lymphadenopathy in advanced stages of malignant melanoma

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Introduction

High-resolution lymph node (LN) sonography in patients with malignant melanoma is a routine diagnostic procedure in medical centres. Its aim is the early detection of lymph node and subcutaneous metastases in relation to tumour stage. LN sonography exhibits a high acceptance when compared with other diagnostic techniques, with good accessibility of the lymph node stations under investigation (J Dtsch Dermatol Ges. 2013 Aug; 11 Suppl 6:1-116, 1-126. doi: 10.1111/ddg.12113_suppl. Malignant melanoma S3-guideline “diagnosis, therapy and follow-up of melanoma”). These follow-up investigations not only result in the early detection of a relapse, they also help to prolong overall survival. In addition, during the same session suspect lymph nodes can be biopsied using FNAC (fine-needle aspiration cytology).

Confirmed metastases must be surgically removed as soon as possible (Schäfer et al. Expert Rev Anticancer Ther. 2007). While the neck, axilla and groin are regarded as regions for investigation that are particularly easily accessible, this strategy can be applied to numerous LN changes other than LN metastases. Sentinel biopsy for example is a further important procedure after sonographic assessment of the relevant LN.

Sonographic criteria

Established sonographic criteria include LN dimensions in relation to the region of the body and the so-called longitudinal/transverse diameter ratio (= Solbiati index, >2), which essentially describes the transformation from an oval to a spherical shape. The blurred margins of the LN, a potential capsular rupture, necrosis or

displacement/broadening of the anatomical structures of the hilum and the cortex can be recorded using B-image sonography (Fig. 1, Table 1). The peripheral tree-like branching of hilar vessels is also regarded as an important diagnostic criterion. Increased vascularisation in reactive lymphadenopathy with preserved vascular structure is particularly characteristic. Cut-offs, displacement of vessels into the margins or the increase in the chaotic nature of the vascular pattern can be differential diagnostic indicators of LN metastases. However, due to the technical limitations of colour-coded Doppler sonography (CCDS) and power Doppler (PD), only the macrovascular architecture is visualized. While these techniques can be used to visualize normal larger hilar vessels, the analysis of the microvessels remains difficult even in contrast-enhanced ultrasound (CEUS) – which

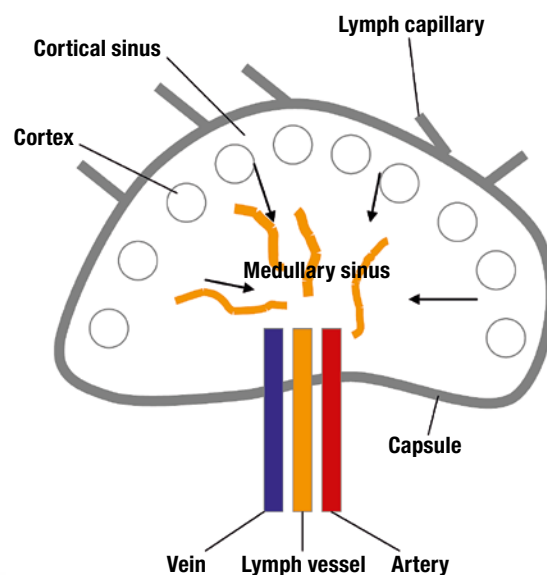


Fig. 1: Schematic illustration of the LN anatomy

2 SMI – a new technique for the analysis of the microvascular tree in reactive and suspected malignant lymphadenopathy in advanced stages of malignant melanoma

moreover incurs additional costs. Analysis of the vascular architecture is particularly complicated in the case of small LNs (<5mm) (Cui, XW et al. Worl J Gastroenterol 2013). Superb Microvascular Imaging (SMI), whose basic principles will be briefly explained below, is a novel sonographic technique to complement CEUS and elastography. Drawing on an initial group of patients with malignant melanoma, typical examples are described where B-mode imaging, CCDS, PD and SMI, as well as elastography were performed.

Superb Microvascular Imaging (SMI)

SMI is based on a powerful intelligent algorithm, applying a similar concept to that used for ultrasonic Doppler signals. SMI effectively separates flow signals from overlaying tissue

motion artefacts, preserving even the subtlest low-flow components with unmatched detail and definition.

1. Doppler signals

Both blood flow and tissue motion (clutter) produce ultrasonic Doppler signals. The strong clutter signals overlap the low-velocity blood flow components.

2. Conventional Doppler imaging

Conventional Doppler imaging applies a wall filter to remove clutter and motion artefacts, resulting in a loss of low-flow components.

3. SMI

SMI does not primarily focus on Doppler shift or the strength of a specific signal, but on its local

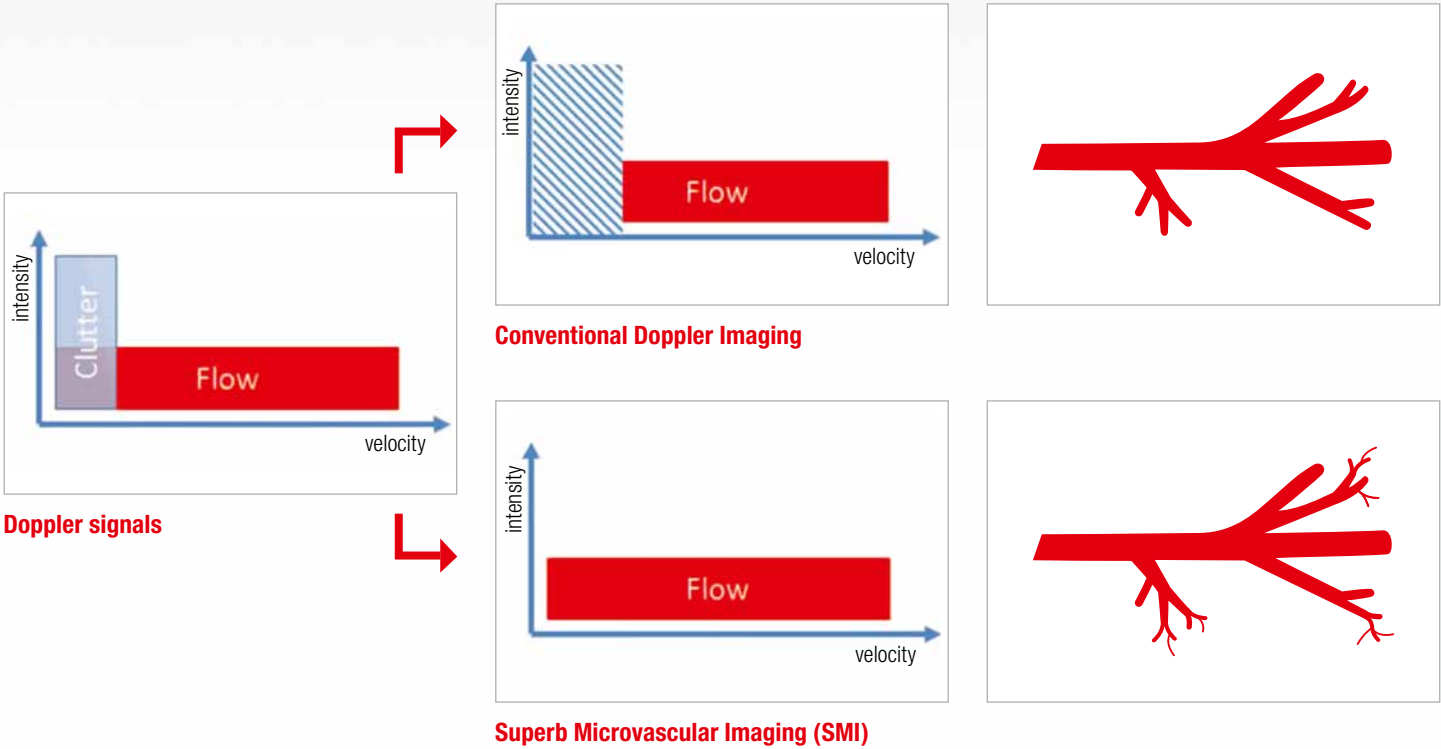
distribution across the region of interest. While tissue motion occurs simultaneously across a region, blood flow always occurs locally. High-density ultrasound system architecture with real-time application capability allows the system to identify and remove global motion signals in real time, while preserving subtle low-flow components.

Non-interventional study

To date, 10 patients have been included in an initial non-interventional study. The SMI technique was used in addition to the standard programme involving B-image sonography, CCDS, PD and FNAC on the Aplio 500 ultrasound system. All patients had a confirmed Clark's Level III-IV melanoma and were treated as part of follow-up. In 3 out of 10 cases, the primary diagnosis that

	Benign	Malignant
Form	elongated oval	round to round-oval, spherical
Solbiati index (longitudinal/transverse diameter)	> 2	< 2
Margins	sharp	partially blurred, partially sharp
Cortex	narrow with low echogenicity	absent or asymmetrically hypoechoic
Centre	relatively homogeneous, high echogenicity	inhomogeneous, hypoechoic
Hilum	usually present on image	absent/asymmetric

Table 1: Differentiation criteria for lymph nodes that have undergone inflammatory or metastatic change



had been made previously was changed based on vascular detection using SMI and this change was confirmed by FNAC and surgical excision. In 7 out of 10 cases, the images of the finest vascular networks generated with SMI were subjectively superior to those generated by the standard techniques, CCDS and PD. This applied both to reactively enlarged LNs (Fig. 2 A–E) and to metastases (Fig. 3). The vascular architecture of superficial and small LNs, in particular, was easier to assess using SMI (Fig. 4). Up to a penetration depth of 2.5 cm and, in particular, in subcutaneous locations, SMI exhibited clear advantages in delineating the hilar vessels and the smallest of peripheral branches. Surprisingly, SMI detected microvessel in portions that had previously been classified as avascular or necrotic, and a targeted

FNAC was immediately performed (Fig. 4). A subcutaneous manifestation was found in 2 of the 10 patients in the region of the scar. The assessment was initially difficult due to postoperative seroma but detection of vessels was particularly important in these cases in order to be able to carry out a FNAC as quickly as possible. The investigation was performed in the frequency range of between 14 and 18 MHz, depending on penetration depth. In the case of suspected malignancy, elastography was carried out on the suspect area of the affected LN. It revealed a good correlation between the absence of elasticity and the presence of bizarre vascular patterns produced by the melanoma metastases (Fig. 5). Furthermore, SMI was able to visualize vessels that pass through the capsule; another

important detail for the assessment of potential metastatic spread that conventional techniques did not offer.

In summary, SMI, which can be used with or without contrast agents, constitutes a novel and promising technique for visualizing microcirculation. In an initial non-interventional study, additional information was found in 3 of 10 cases that had not been detected previously using the conventional techniques CCDS and PD. In particular, SMI provided relevant information that allowed the evaluation of small lesions, subcutaneous masses and structures in the region of the scar.

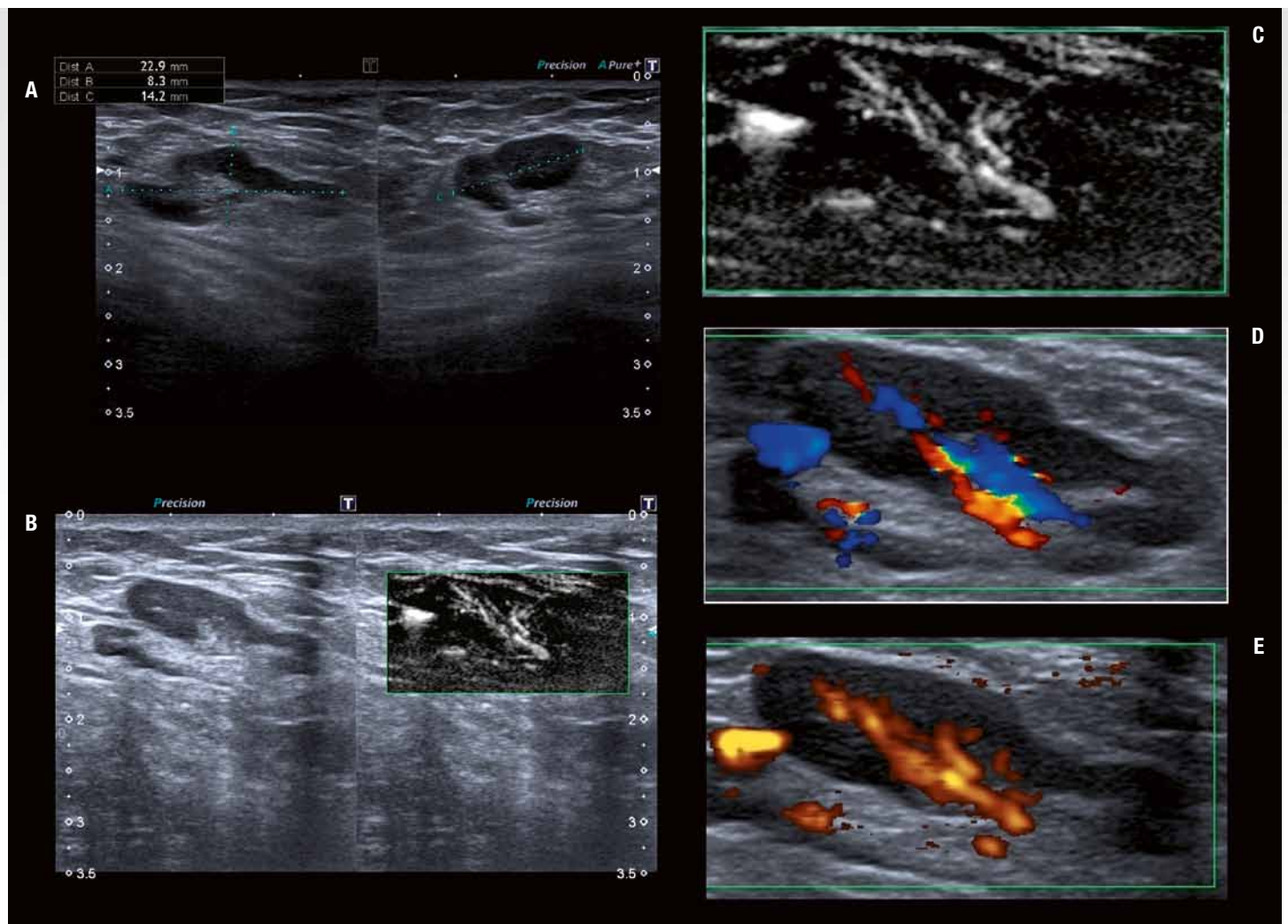


Figure 2 A–E: Right axillary reactive lymphadenopathy (A). Unremarkable finding in FNAC. Illustration of the full vascular tree with its microarchitecture in SMI mode (B, C). The large vessels close to the hilum are seen in CCDS (D) and power Doppler (E), the vascular tree is not free of artefacts and its detection is limited.

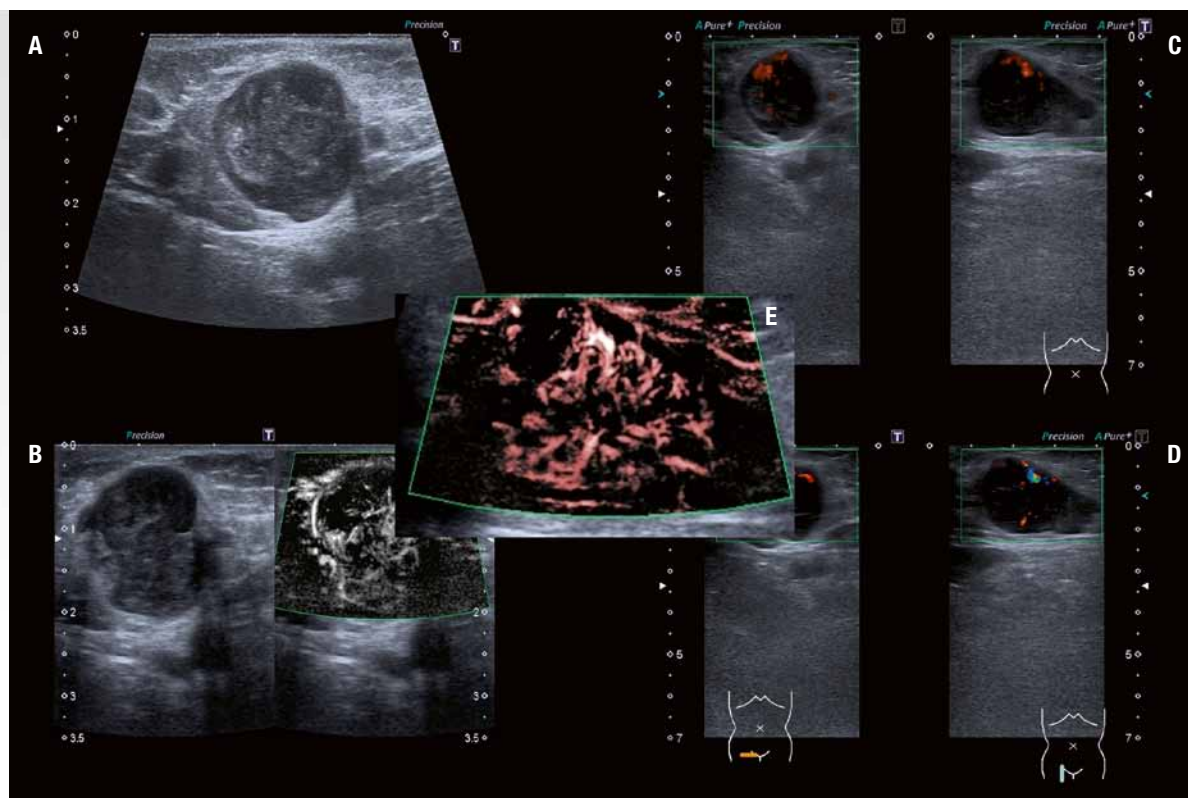


Figure 3 A–E: Large right inguinal LN metastasis that has been histologically confirmed (A). The pathological vascular pattern and the vessels passing through the LN capsule are visualized only by SMI (B). Power Doppler (C) and CCDS (D) only allow delineation of the macrovessels. In this case, no change in the diagnosis was to be expected based on the clear situation. Of note, however, is the level of detail visible in the microvessels and the fact that very fine vessels have broken through the capsule (E). The sensitive, artefact-free image produced by SMI of pathological vascular networks is well documented in this figure.

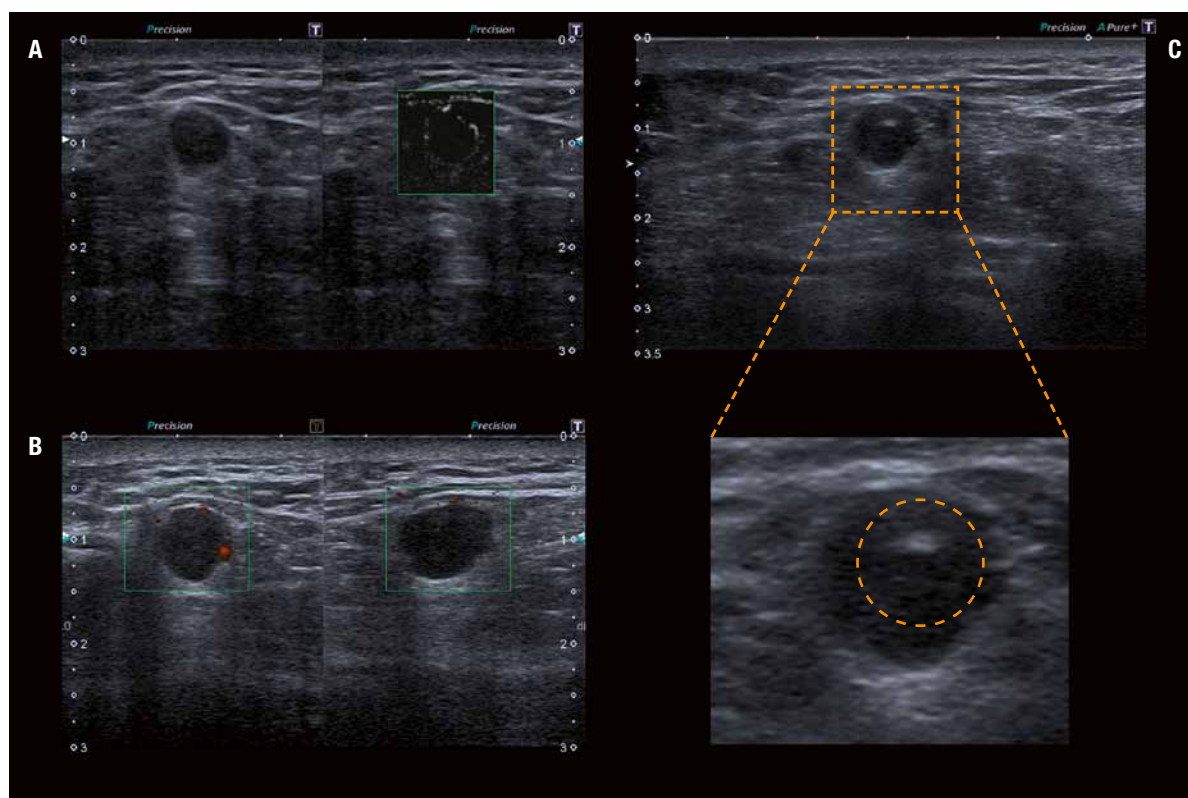


Figure 4 A–C: 6 mm metastasis adjacent to the region of the scar on the right thigh. Vessels with branching in the margins are visualized by SMI, while the lesion appears avascular in power Doppler. Metastasis confirmed with FNAC (C).

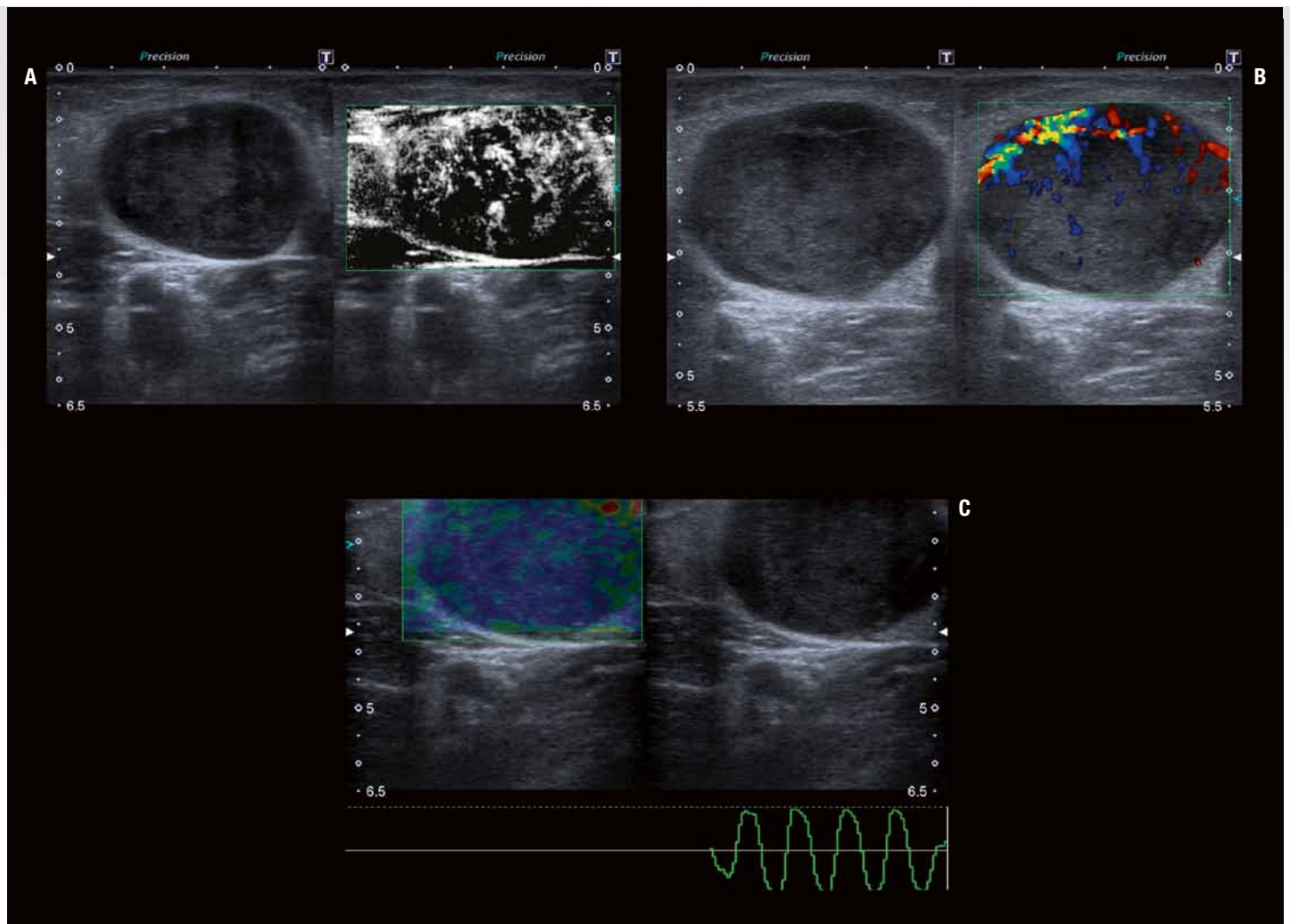


Figure 5 A–C: Correlation between SMI (A), colour Doppler (B) and elastography (C) for a large LN metastasis. SMI visualizes the finest tumour vascular networks.

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