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Images of Spinal Nerves and Adjacent Structures With Optical Coherence Tomography: Preliminary Animal Studies

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Abstract: Multiple complications have been reported with spinal intervertebral transforaminal injection procedures, despite the use of fluoroscopic needle-positioning measures. We explored an imaging technology (optical coherence tomography, or OCT) for its possible use in spine interventional procedures as a means of providing needle tip vision at the neuroforamen. Optical coherence tomography is the B-mode optical analog of ultrasound. With the use of 2 different (time- and frequency-domain) OCT systems, we obtained high-resolution (~10 μm) images of ex vivo and in situ paraspinal structures (spinal nerves, radicular artery, dura, cauda equina) in different animals. An OCT forward-looking, needle-shaped endoscope in development is presented, with a discussion of its possible method of use, safety, efficacy, technical problems, and future prospects. Further studies are needed to determine whether such OCT technology has a potential niche in the performance of spine pain procedures.

***Perspective:** This article presents preliminary high-resolution images obtained with an optical imaging approach (optical coherence tomography) of neurovascular and other structures within the spinal neuroforamen. Advances in this technology may provide effective needle tip vision for pain interventionalists and may help to reduce complications from spine needle injection procedures.*

***Key words:** Complications, intervertebral foramen, optical coherence tomography, imaging, radicular artery, medullary artery, spinal nerve root, dura.*

Cervical radicular pain, for which disc herniation and foraminal stenosis are the major causes, is believed to originate from nerve inflammation. This is the basis for injecting steroids in conjunction with local anesthetics. The use of an intervertebral transforaminal route, as opposed to an interlaminar approach, allows the direct delivery of steroids and local anesthetics onto the target nerve. However, major complications have been reported with needle injection into the spinal neuroforamen despite the use of fluoroscopic needle-positioning measures.[10,11] An imaging technology is needed whereby needle tip vision is achieved of critical neurovascular and other structures at the injection site. With such a capability, complications would be minimized, and the risk of failure of intended therapeutic effects would be lessened. We review below the complications and current safety limitations of current intervertebral transforaminal injection techniques, and how these concerns might be addressed with a developing optical imaging method, called optical coherence tomography (OCT).

Serious neurologic complications and deaths[20] have been reported with cervical injection procedures, including severe anterior spinal artery syndrome with fatal spinal cord infarction,[4] bilateral cortical blindness owing to left vertebral artery puncture due to air/contrast dye injection,[18] quadriplegia,[1] complex regional pain syndrome secondary to nerve root needle trauma,[22] and fatal perforation of the left vertebral artery.[21] Many more cases are known to have occurred, but have not been reported in the literature for medico-legal reasons. Hence, the complication prevalence rate is unknown, but it is believed to be significantly higher than procedures performed in the lumbosacral area.

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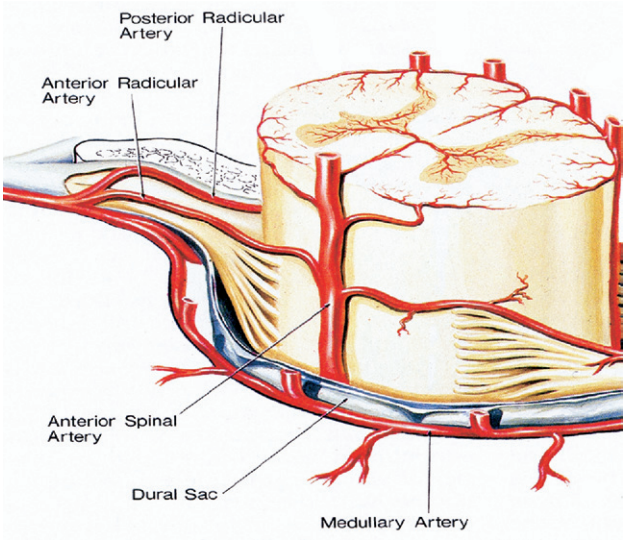

Figure 1. Arterial supply of the spinal cord, with radicular and medullary arteries. Reprinted with permission.[7]

The likely cause of many such neurologic injuries is compromised perfusion in a radicular or medullary artery[2] (Fig 1). Particulate material in depot preparations of corticosteroids, or injected air, can serve as emboli that can be injected directly into an artery, or that can be alternatively pressurized through a vessel puncture site. The introduced emboli occlude the radicular or medullary artery and infarct the spinal cord.

In the Discussion section, we review the safety limitations of current intervertebral transforaminal injection techniques, and how these concerns might be addressed with a developing optical imaging method, called optical coherence tomography (OCT).

OCT is the optical analog of B-mode ultrasound. It is a laser-based imaging modality that uses visible laser light to nondestructively image subsurface tissue structures, such as nerves, fat, muscle, blood vessels, and cartilage. The technique[15] is based on comparing light reflected from objects to a reference signal to determine depth penetration (interferometry). With a Michelson interferometer, OCT measures the amount of the interference obtained from different points within the tissue by moving the mirror in the reference arm, which changes the distance light travels in that arm. Two- and three-dimensional images are produced by scanning the beam across the sample and recording the reflection as a function of transverse position.

Optical coherence tomography allows imaging through most tissues, including nerves and arteries, to a depth of up to 2 mm with good resolution (~10 μm).[3,6,9] Although this would appear to be a very limited viewing depth, it might be sufficient to allow identification of key neurovascular structures located immediately at the needle tip before injection. For pain interventionalists, a 1- or 2-mm change in location can make a significant difference complication-wise. It follows that if OCT could image key structures near the needle tip, neural injury could be avoided by slightly withdrawing the needle.

We present data obtained from preliminary ex vivo and in situ animal studies (dog, pig, rabbit, cow), with the purpose of identifying OCT image features of critical structures (nerve, vessel, dura) in front of a forward-looking OCT imaging system. The images were obtained with 2 different forward-imaging OCT systems: (1) a frequency-domain OCT imaging system developed at the California Institute of Technology and (2) a time-domain Niris Imaging System (Imalux, Cleveland, OH) with the use of a portable handheld 2.7-mm diameter probe.

Materials and Methods

California Institute of Technology Swept Source Frequency-Domain Imaging System

The frequency-domain OCT (FDOCT) engine employed in this experiment is based on a swept laser source (Micron Optics si425-1300SL; Micron Optics Inc., Atlanta, GA). The OCT light source, which had a central wavelength of 1310 nm with a bandwidth of 70 nm, was coupled to a fiber-based Michelson interferometer. Axial line scanning rate was 500 Hz. This system was used for ex vivo studies, with the dissected specimens placed in the imaging well of the system. The forward-looking OCT beam, in micrometer translational steps, scanned the fixed-position specimens in transverse and longitudinal views.

IMALUX NIRIS Time-Domain System

The Niris Imaging system from Imalux Corporation is a compact desktop, time-domain, forward-imaging OCT system that uses low-coherent broadband light in the near infrared range. Its scanning depth is 2.2 mm in air, and its lateral scanning range is 1 mm. Image acquisition rate is at 1.5 seconds/frame. It uses a 2.7-mm outer diameter reusable, handheld imaging probe, which was placed atop structures of interest to generate the images for in situ studies.

Animal Studies

All animal studies were performed with approval of the Animal Care Institutional Review Boards of the University of Southern California and the California Institute of Technology. All dissections were performed by a neurosurgeon, with careful exposure of paraspinal structures of interest. Epidural and spinal needles were used to create dural punctures, respectively, in a euthanized pig and rabbit. Dissected spinal nerve roots and radicular arteries in the intervertebral foramen region were studied in the same animals. The bovine cauda equine was studied, as were canine brachial plexus nerves.

Results

Dural Defects

Ex Vivo Pig Study

In a 25-kg euthanized pig, surgical dissection was performed through the midline lumbar region down to the

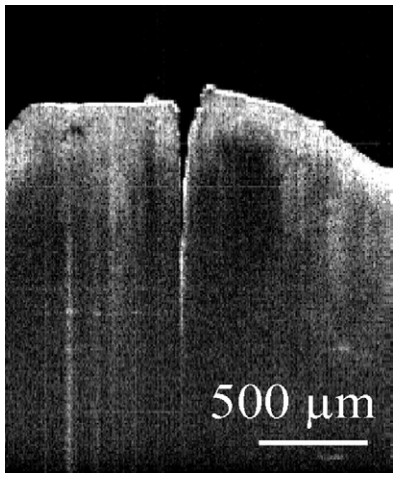

Figure 2. Optical coherence tomography image of dural defect caused by puncture with 17-gauge Tuohy needle.

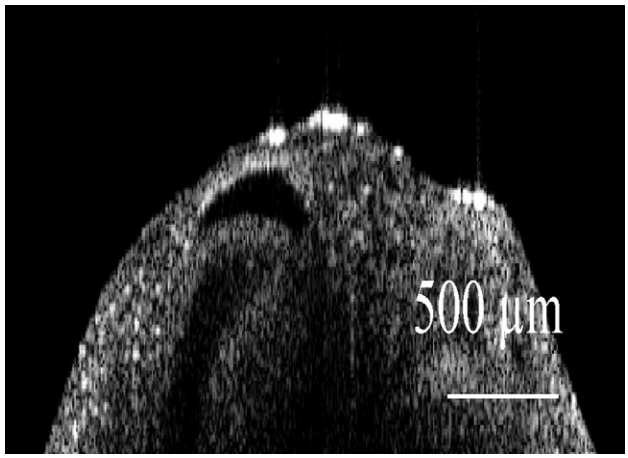

Figure 4. Frequency-domain optical coherence tomography image of a porcine epineurial vessel atop a porcine spinal nerve root.

level of dura, along the pathway of an epidural needle midline approach. A dural specimen was excised, and the ex vivo specimen was fixed in position, punctured with a 17-gauge Tuohy epidural needle, and placed in the imaging well of an FDOCT system. The baseline intact dura reveals an essentially uniform tissue. Subsequent to puncture with the epidural needle, the effect on the dura is evident as a significant conical defect (Fig 2). Imaging was performed with the CalTech system.

In Situ Rabbit Study

Dissection was performed on a euthanized 10-kg rabbit down to the lumbar dura, along the pathway of a spinal needle midline-approach. We performed successive dural punctures with a 26-gauge needle. Each puncture produced an evident discontinuity in the high scattering dural layer when visualized using OCT (Fig 3). The lateral size of the dural defect (370 μm) was comparable to the needle tip (400 μm). No similar defects were seen in the intact (unpunctured) dura. The dura in the rabbit measured 43 μm in thickness. OCT imaging was done with the time-domain Niris System.

Nerve Roots/Radicular Artery

Ex Vivo Pig Study

Dissection was done to expose the lumbar spinal nerve roots in the neuroforamina of the euthanized pig. With the FDOCT system, we obtained ex vivo images of a porcine radicular artery (Fig 4), which longitudinally followed the course of the spinal nerve root, and which was located on the posterior surface of the nerve. It has a muscularis layer, compatible with that of an artery. Of special note is the small size of the subsurface vessel (~500 μm). On the right hand side, in Fig 5, the corresponding hematoxylin and eosin stain reveals the same epineurial vessel, its half-moon shaped lumen partially filled with blood.

In Situ Rabbit Study

Dissection was done to expose the spinal nerve roots in a euthanized rabbit. No radicular vessel on a spinal nerve root was grossly seen during the rabbit dissection; how-

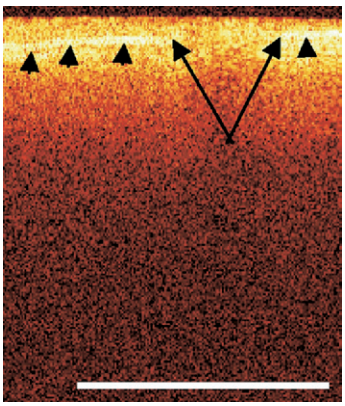

Figure 3. Dural puncture in rabbit spinal cord with 26-g needle. High scattering horizontal structure with sharp contrast (arrowheads) is the dura, which measures 43 μm in thickness. A dural defect measuring 370 μm is identified (arrows).

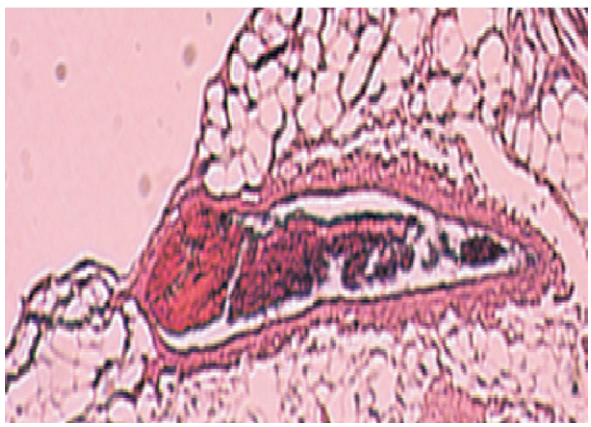

Figure 5. The same epineurial vessel as in Fig 4 after staining with hematoxylin and eosin.

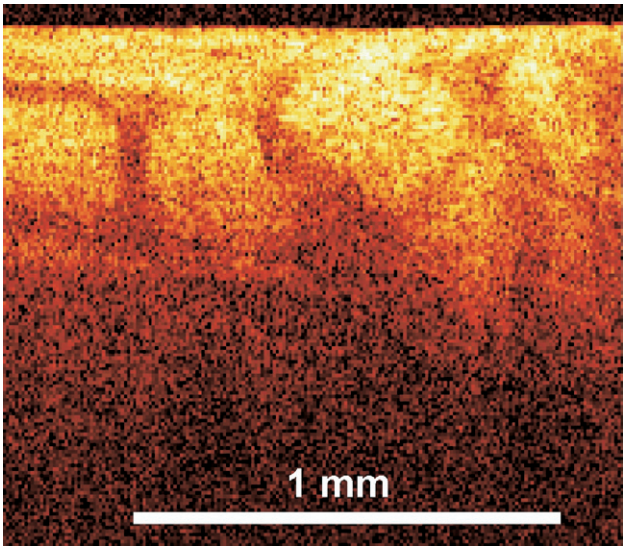

Figure 6. Optical coherence tomography image of ex vivo bovine cauda equina. Nerve roots appear as distinctive and homogenous round to oval structures averaging 300 μm in diameter.

ever, additional OCT images revealed the presence of subsurface radicular vessels measuring approximately 260 to 300 μm in diameter.

Spinal Nerve Roots

Ex Vivo Cow Study

The distal spinal cord and intact cauda equine of a cow was examined ex vivo. Fig 6 shows a transverse cross-sectional OCT image of the bovine cauda equina. Multiple nerve roots are evident as round to oval homogeneous structures, with an average diameter of 300 μm. The corresponding histologic image (Fig 7) shows 4 hematoxylin and eosin–stained round to oval nerve roots with intact epineurium. The hematoxylin and eosin–stained section confirms the homogeneous nature of the

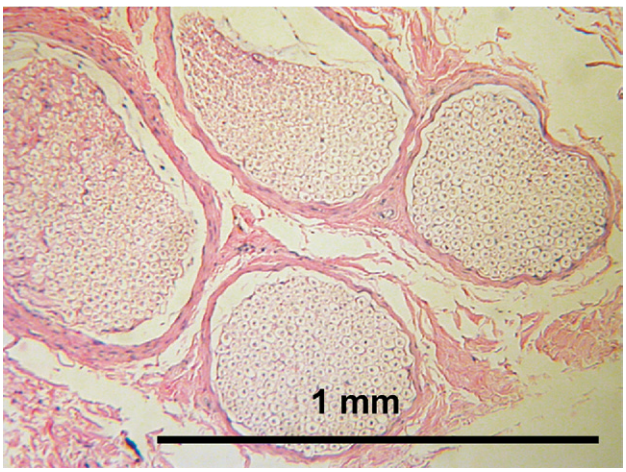

Figure 7. Histological image of ex vivo bovine cauda equina. Four nerve roots are seen corresponding to the OCT image of Fig 6. Dozens of individual nerve fibers are seen in each nerve root. Hematoxylin and eosin stain.

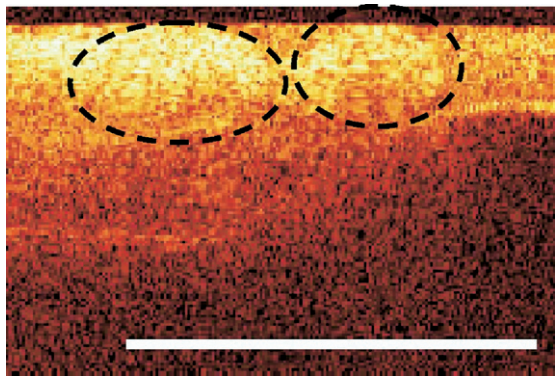

Figure 8. Optical coherence tomography image of a rabbit spinal nerve root. Root is shown as it split into 2 distinct branches outlined by dashed lines. Bar is 1 mm.

contents of the spinal nerve roots, each of which contains dozens of individual nerve fibers.

In Situ Rabbit Study

The time-domain system was able to visualize the lumbar spinal nerve roots, which were evident as bright homogeneous structures (Fig 8).

Peripheral Nerve

In Fig 9, 1 has the hematoxylin and eosin–stained section of a transversely cut ex vivo canine brachial plexus nerve. A multitude of myelinated nerve fibers occupy the interior of the nerve. Each nerve fiber consists of a central axon surrounded by a myelin sheath.

Fig 10 shows the corresponding OCT transverse image, with its similarly arrayed multitude of dark ovoid structures (nerve fibers), each fiber surrounded by a thin, lightly colored rim. This study was done with a polarization sensitive OCT (PS-OCT) system.[19] In studies of nerve fascicles from the brachial plexus, the nerve fibers within the fascicle course not only parallel to the direction of the fascicle but also laterally within the fascicle, as suggested by the upper portion of the figure. In the longi-

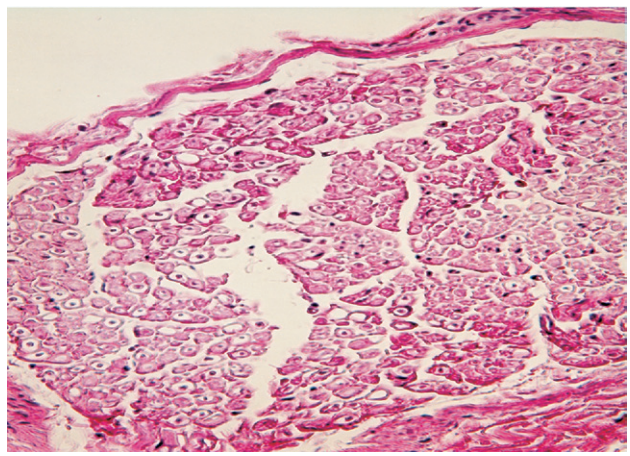

Figure 9. Hematoxylin and eosin–stained transverse cross section of a canine brachial plexus nerve. Magnification ×45 to 50.

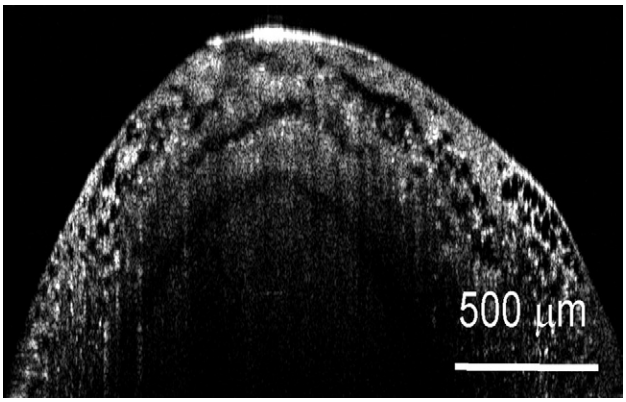

Figure 10. Optical coherence tomography image of transverse cross section of a canine brachial plexus peripheral nerve.

tudinal view, as shown in Fig 11, the nerve fibers are seen as dark tortuous tubular structures that parallel the course of the nerve.[25]

Discussion

The limitations of safety measures used to minimize such complications are:

(1) *Inability of Fluoroscopy to Image the Spinal Nerve and Radicular Artery*. Fluoroscopy cannot image the spinal nerve roots, nor can it image the radicular/medullary artery except when there is accidental arterial injection of contrast dye.[20]

(2) *Unreliable Blood Aspiration Test*. In both cervical and lumbosacral ESIs, a positive flash or aspiration of blood is only predictive of intravascular injection in less than half of the documented intravascular responses (~45% false-negative rate). Therefore, aspiration before injection is not a consistently reliable means of preventing needle intravascular placement.[10,11,14]

(3) *Individual Deviations From Presumed Working Anatomy*. Practice guidelines for safe cervical transforaminal procedures urge operators to place the needle posteriorly in the intervertebral foramen dorsal to the spinal nerve in order to avoid any arteries, on the assumption that these vessels lie anterior to the spinal nerve[5,24] (Fig 1). The presumed working anatomy is that, above the equator, the needle may encounter epiradicular veins, whereas below it, it may encounter the spinal nerve and its arteries. However, 1 study[8] has demonstrated that radicular arteries can be seen posterior to the spinal nerves, 1 lying high and the other lying low in relation to the spinal root. The extent of such individual variation is unknown. Hence operators cannot rely on the presumed working anatomy as an absolute guarantee of procedural safety.

(4) *Discontinuous Imaging of Target Site*. A test injection of contrast medium is considered mandatory. But an operator may easily miss the fleeting image of a thin radicular artery branch upon injection. Moreover, an inadvertent intra-arterial injection might still occur after an ever so slight movement of the operator's hand, or even with a minimal displacement of the syringe needle or of the volume tubing subsequent to the digital angiogram. This is a significant limitation of discontinuous imaging.[14]

(5) *Nonfusion of Midline Cervical and High Thoracic Ligamentum Flavum*. For interlaminar midline approaches with spinal needle procedures, the loss-of-resistance technique relies on a perceptible penetration of the ligamentum flavum. In a study of 52 human cadavers, mid-line gaps in the ligamenta flava are frequent at cervical (>50%) and high thoracic levels (2% to 20%) but are rare at the T3 level and below. Hence, one cannot rely on penetration of the ligamentum flavum as a perceptible barrier to interlaminar cervical placement of an epidural needle.[17]

OCT Image Results

With FDOCT imaging in a pig, the dural defect produced by the 17-g Tuohy needle has the shape of a cone. The defect is widest at the surface, and extends to an intradural depth of 1.2 mm. The subsurface extension of the defect is not evident in conventional en face electron micrographs that show the defect frontally. It should be noted that the spinal dura mater is a tube of dense connective tissue that is generally not very vascular, except for tiny twigs from the spinal arteries. Hence, intradural vessels in these images are not seen, as expected.

With an in situ 26-gauge dural puncture in a rabbit, the defect appears as a discontinuity in the dura. The defect fills up with underlying cerebrospinal fluid. In comparison to the pig epidural defect, the spinal needle defect is not as evident in the depth direction.

The radicular artery is a critical feature that a pain interventionalist must recognize in order to avoid intravascular injection while advancing the needle in the transforaminal region. A porcine epineurial vessel is clearly imageable on top of a spinal nerve root in Figs 4 and 5. The evident musucularis layer distinguishes this structure as an artery, which is surrounded by fatty

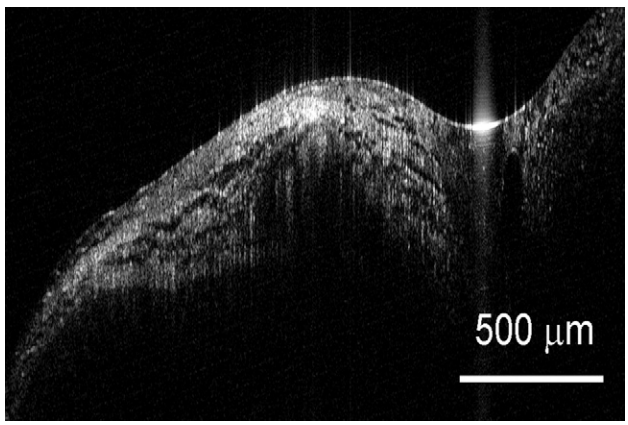

Figure 11. Optical coherence tomography longitudinal view of brachial plexus peripheral nerve.

tissue, and which very likely is the posterior branch of a radicular artery. The crescent moon shape is compatible with the appearance of extrinsic nutrient arterial vessels that reach the epineurium, ramify within the outer layer, and supply the intraneural plexus through ascending and descending branches.

As shown in earlier studies,[3] OCT can be used to identify nerve fascicles, a characteristic and defining feature of peripheral nerves. An individual nerve fascicle, depending on its location and function, can be monofascicular, bifascicular, or polyfascicular. With a higher resolution OCT system, it may be possible to image nerve fibers within the fascicles. Fig 10 shows a canine brachial plexus nerve with a honeycomb of myelinated nerve fibers in transverse cross-section, confirmed by hematoxylin and eosin staining (Fig 9). In longitudinal cross-section (Fig 11), a pattern of sinuous and tortuous parallel tubular tracts is evident. Tortuosity of the ex vivo fascicles within the nerve occurs because the elastic and normally stretched nerves retract upon excision.[19] With high-frequency ultrasound, the same tortuous pattern is seen in longitudinal images of ex vivo nerve specimens.[25]

Proposed Imaging Approach

For pain specialists, the basic question is whether OCT imaging can prevent neural injury. Prior investigations indicate significant neural injury results when a needle penetrates through the fascicle, and even more so when local anesthetic is injected into the fascicle.[12] In contrast, little or no injury occurs when the needle path, even with local anesthetic injection or infusion, is extrafascicular, that is, into the epineurium.[13,23] Certainly, if a nerve fascicle is seen at the tip of a forward-imaging OCT needle endoscope, it would make sense to withdraw the needle slightly.

What about injection into a vessel? For an artery, OCT can image the wall layers of the vessel, and allow its ready identification as such. Distinguishing an epineurial artery from a vein would require observing the thickness of the muscularis layer.

Hence, given the limited depth window of OCT, for an image of the tissue in the immediate vicinity of the needle tip, is the combined absence in the OCT image of a vessel and the absence of nerve fascicles a sufficiently protective measure against neural harm? The preliminary evidence presented herein allows us to think so. First, the conventional radiological guidance methodology could be employed to optimally position the needle tip. Second, OCT could be used to explore the proposed injection site, if need be, to determine whether a vessel or nerve was in the immediate vicinity. If a nerve or vessel was noted, the needle could be repositioned such that no neurovascular structure was present in the OCT image, indicating at least a 2-mm margin of safety, for which the risk of an intraneural or intravascular injection should be nil. On a cautionary note, we note that other imaging techniques have been proposed in which the absence of a single end point was deemed as safe, yet subsequent clinical usage revealed that it was found to be insufficient to provide complete safety or protection.

Optical coherence tomography has significant limitations. It is unlikely that it can be used as a major guidance method to direct the needle from skin to final foraminal injection site. For example, if the needle tip is 1 to 2 cm away from the target site, the narrow OCT imaging depth window of 2 mm may not reveal any identifiable reference structures in the spinal foraminal area. Careful half-millimeter-sized movements of the needle would be needed to bring reference structures into view. The most suitable role of OCT would then seem to be to combine it with standard radiological positioning, and then to use it as an exclusionary high-resolution device for the final end positioning. At the very end, OCT could be used to exclude the possibility of any injection into a critical neurovascular structure. Such an approach might be superior to conventional blood aspiration and dye injection tests that have not proven to be sufficiently protective.

Present studies indicate that the effective imaging depth of OCT can be extended. Adaptive ranging[16] (AR) is a dynamic feedback technique currently in development whereby image data are used to adjust the OCT system coherence gate offset, improve dB sensitivity, and extend the imaging range to as much as 7 mm. If this extended imaging range is consistently attainable with AR-equipped OCT systems, OCT as an imaging modality would become much easier to use.

The major remaining limitation is thinness of the imaging probe. Current research is proceeding toward the creation of even thinner OCT needle probes. Ideally, it would seem that practitioners need a 25-g forward-looking OCT needle for cervical foraminal injections. However, the smallest forward-looking OCT imaging needle currently in existence is a frequency-domain 21-gauge imaging needle developed at CalTech.[26] This is close in size to a 22-gauge spinal needle, which is used often in lumbosacral spinal injection procedures. However, it may be otherwise argued that the use of a 25-gauge needle may make it easier to enter the small vessels near the neuroforamen, although there is no convincing evidence collected in a prospective randomly way to justify preference of a slightly larger needle versus a small needle.

Any such OCT needle probe, with its internal optical fiber incorporated into the needle, would also require a conduit for the administration of injectate. In its proposed design, the OCT needle endoscope would allow needle tip visualization of the actual site of injection and of the local spread of the injectate.

These preliminary animal experiments suggest a potential niche for an OCT-based imaging needle in the performance of spinal foraminal injections. However, many more investigations involving humans are required before OCT can be recommended for routine use. An extensive OCT neuroforaminal image database first needs to be created, in order to better appreciate

the effects of individual variation and disease processes. If the OCT imaging range can be extended, as with adaptive ranging, the training curve in the use of this technology should be no greater than that associated with ultrasound.

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