Welcome to another talk in André Boezaart’s “Must-know anatomy for regional anesthesia and acute pain medicine” lecture series. This lecture is an outline of the Microanatomy of Peripheral Nerves.
The author is André Boezaart, a Professor of Anesthesiology and Orthopaedic surgery at the University of Florida College of Medicine.
The microstructure of all the mixed nerves in the axilla is similar. We consider the ulnar nerve here as an example of a nerve in the axilla. It is an example of a single nerve …
... in its own circumneural sheath (also called the paraneural sheath), and like any other mixed peripheral nerve, ...
... the ulnar nerve comprises numerous fasciculi, ...
… each surrounded by a dense perineurium ….
…. and held together by a looser epineurium.
The *endoneurium*, which is marked here as number 12, is a fine cylindrical lamina that encloses groups of axons with their respective Schwann cells.
The axons consist of different axon fiber types, depending of the type of nerve in question. Both myelinated …
... and unmyelinated axons are surrounded by collagen fibers of the endoneurium, but the endoneurium is permeable and thus does not interfere with molecule passage.

The single-layered endothelial cells of the capillaries in the endoneurium contribute to the blood-nerve barrier. The term endoneurium is sometimes incorrectly used to denote the intrafascicular compartment of the nerve, but its use should be restricted to refer to intrafascicular connective tissue, excluding the perineurial partitions that may subdivide fascicles. Approximately 40% to 50% of the intrafascicular space is occupied by non-neural elements and anywhere from 20% to 30% of this is endoneurial fluid (cerebrospinal fluid) and connective matrix – the
The *perineurium* (#11) comprises multiple single-cell layers …
… that enclose individual nerve fascicles (#10). They become progressively thinner as the number of fascicles increase.

As Key and Retzius described in 1878, the essential structure of the perineurium is a lamellated arrangement of flattened cells separated by layers of collagenous connective tissue that provides an ensheathment for somatic and peripheral autonomic nerves and their ganglia. The cellular lamellae comprise concentric sleeves of flattened polygonal cells that are equipped to function as a metabolically active diffusion barrier, although they do not have the morphologic features of a true epithelium. It is a continuation of the dura mater that surrounds the spinal cord and is a tough and non-compliant structure.
The **epineurium**, marked as number 9 consists of a condensation of areolar connective tissue that surrounds the perineurial ensheathment of the fascicles of uni- and multifascicular nerves. The attachment of the epineurium to surrounding connective tissue is loose, allowing the nerve to be relatively mobile except where tethered by entering blood vessels or branches. Greater amounts of connective tissue are normally present where nerves cross over joints. In general, the more fascicles there are, the greater the quantity of epineurium. The epineurium most likely originates as a continuation of the paravertebral fascia.
Variable quantities of adipose tissue are also present in the epineurium, particularly in the larger nerves. After studying the distribution of fat in human nerves and finding predominance in the sciatic nerve, researchers feel that this tissue probably has a protective function in cushioning the fascicles against compression injury. The susceptibility to compression injury is likely to be less in large multifascicular nerves with considerable quantities of epineurium and fat than in smaller and unifascicular nerves.
The *vasa nervorum* enter the epineurium, where they communicate with a longitudinal anastomotic network of arterioles and venules. The epineurium also contains lymphatic vessels that are not present within the fascicles. These lymphatic channels accompany the arteries of the peripheral nerves and pass into the regional lymph nodes.
Anderson and colleagues recently demonstrated the \textit{circumneural} (paraneural) sheath in dissections, …
… and Manoj Karmakar and his colleagues described the appearance of the circumneural sheath with high-definition ultrasound – the short arrows in this ultrasound image. In neurosurgical texts, the circumneural sheath it has been known as the “gliding apparatus” of the nerve. We now know that injection of a local anesthetic agent or catheter placement in the subcircumneural space (subparaneural space) is ideal for single-injection and continuous nerve block, respectively.
Reina and colleagues stained sections through the brachial plexus and peripheral nerves with Masson’s trichrome staining to convincingly demonstrate the microscopic ultrastructure of the circumneural (paraneural) sheath – the white arrows on this slide. The red arrow indicates the sub-circumneural space and the green arrows highlight the sub-epimyseal space, which forms the so-called doughnut on ultrasound when injecting a fluid such as local anesthetic agent into it. Please view the lecture on the microanatomy of the brachial plexus for a more detailed discussion of this.
At the level of the subgluteal crease, where a subgluteal sciatic nerve block is usually performed, the sciatic nerve is not a single nerve; rather, it is a bundle of three nerves. The sciatic nerve is an example of a nerve with a number of branches inside a single circumneurium (#6 in this slide). The sciatic nerve, at this level, comprises at least three nerve branches: …
... the tibial nerve, ...
... the common peroneal nerve, ...
… and the muscular branch to the hamstring muscles.
There are significant variations in these arrangements in normal anatomy, but this is the most common arrangement.
All three of these nerves are usually surrounded by a single circumneurium (#6), also known as a paraneurium. Otherwise, it has the same layers of sheaths as other peripheral nerves (#4, #6, #8, & #10).
At the level of the inguinal crease, the femoral nerve is also not a single nerve; rather, it is, as in the sciatic nerve, a bundle of nerves. As an example of a nerve with a number of branches inside a single circumneurium, the femoral nerve is shown here.
Although there is considerable individual variation, the most common arrangement has the nerve to the pectinius muscle (#1a), …
… the medial and intermediate cutaneous nerves of the thigh (#2b)…
… the nerve to the sartorius muscle (#3c), …
... and the four nerves to the four quadriceps muscles (#4d-#7g), ...
... inside the same circumneural sheath.
Otherwise, each individual nerve also has the same layers or sheaths as other peripheral nerves, namely, the epimysium (#4), the epineurium (#8), which most likely originates from the paravertebral fascia and surrounds each individual nerve; the perineurium (#10), which is a tough layer and probably originates from the dura and surrounds each individual fascicle (#9), and the endoneurium (#11), which encloses groups of axons with their respective Schwann cells.
From a microanatomical point of view, it is important to realize that the subcircumneural space (#7) is generally the so-called “sweet spot” of the nerve. The ideal position to place catheters for continuous nerve blocks would be inside this space to prevent secondary block failure.
The sub-epimyseal space (#5) may be ideal for needle placement and injection for single-injection nerve blocks. Local anesthetic agents or other fluid injected into this space forms the so-called “doughnut” around the nerves seen on ultrasound during ultrasound-guided nerve blocks. This is not the ideal place to put a catheter because the low volume and low concentration local anesthetic agent used for continuous nerve blocks, which reaches the axons by diffusing over the membranes against a concentration gradient, cannot reach the axons and this typically gives rise to secondary block failure. The primary block, where a high volume and high concentration are used, is usually successful if the local anesthetic agent is injected into this space. Please refer to the talk on the microanatomy of the brachial plexus for more detail on this.
Thank you for your attention and we look forward to seeing you again soon in another talk by André Boezaart in this series on the minimum anatomical knowledge a practitioner should attain for regional anesthesia and acute pain medicine procedures.
This lecture series was adapted from:

“The Anatomical Foundations of Regional Anesthesia and Acute Pain Medicine: Macro-, Micro-, Sono, and Functional anatomy”.

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