Principle of relative positioning of structures in the human body

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Abstract
The arrangement of various biological structures should generally ensure the safety of crucial structures and increase their working efficiency; however, other principles governing the relative positions of structures in humans have not been reported. The present study therefore investigated other principles using nerves and their companion vessels in the human body as an example. Nerves and blood vessels usually travel together and in the most direct way towards their targets. Human embryology, histology, and gross anatomy suggest that there are many possible positions for these structures during development. However, for mechanical reasons, tougher or stronger structures should take priority. Nerves are tougher than most other structures, followed by arteries, veins, and lymphatic vessels. Nerves should therefore follow the most direct route, and be followed by the arteries, veins, and lymphatic vessels. This general principle should be applicable to all living things.

Key Words
neural regeneration; reviews; principle; position; anatomy; human embryology; histology; neuroregeneration

Research Highlights
This study used nerves and their companion vessels in the human body as examples to investigate the principles governing the relative positioning of structures within organisms. Tougher or stronger structures take priority for mechanical reasons. The results can help to explain the arrangements of local blood vessels and nerves.

INTRODUCTION
There is an accepted principle that the arrangement of structures in the human body should ensure the safety of crucial structures and increase their working efficiency. For example, the nucleus is located in the center of the cell for safety and efficiency. The main arteries lie at flexures, where they receive natural protection⁴. Blood vessels branch from the adjacent main vessel and travel towards their target in the most direct way possible, to maximize efficiency. However, other principles governing the relative positioning of structures in organisms have not been reported.

The present study used nerves and their companion vessels in the human body to investigate the principles governing the relative positions of structures. The general rule⁴, that an artery accompanies its companion nerve on the side from which it approaches it, is broken at several sites in the upper and lower limbs, and the customary⁴ order of the nerve, artery, vein
is not maintained at the popliteal fossa. A reliable principle thus needs to be established.

**HYPOTHESIS**

Studies of human embryology, histology, and gross anatomy suggest that there are numerous possible options for the positions of nerves and their companion vessels during development. Meanwhile, for mechanical reason, tougher or stronger structures take priority. In line with this generalization, a wide choice of positions for nerves and their companion vessels exist during development, with nerves being the toughest element, followed by the arteries, veins, and lymphatic vessels. Nerves should therefore take the most direct route, followed by the arteries, veins, and lymphatic vessels, respectively. This principle should be applicable to all living things.

**EVIDENCE**

**Human embryology and histology**

(1) During development, networks of blood vessels sprout into actively-growing parts (e.g., organs and limbs) and gradually advance further into them. There is a wide choice of channels in the network, some of which are selected to be occupied by permanent arteries and veins and their branches; the rest of the network either disappears or remains to accommodate branches of the blood vessels. The force of the blood eventually causes the chosen path to straighten; however, if some of the branches are firmly anchored, the blood vessel may be compelled to adopt an angular or zigzag course\(^1\). Some arteries, such as the facial and the uterine arteries, follow a tortuous course to accommodate changes in the shape of their target structure. Lymphatic vessels develop in a similar manner to blood vessels, but about 2 weeks later\(^2\).

(2) Specific molecular cues guide axons to their targets\(^3\). Each newly-growing nerve fiber bears an amoeboid tip that projects searching pseudopodia into the interstices of the tissue through which the fiber is growing. Each tip moves along, guiding its fiber behind it. Once a few fibers have traversed a region, many other fibers follow along these to form a nerve bundle. The path of the nerve bundle will be reasonably straight in embryonic tissues, though obstacles such as blood vessels and supporting elements can cause temporary or permanent deviations\(^4\).

(3) Somatic nerves are cord-like and relatively strong, because peripheral nerves have a fairly extensive connective tissue component\(^5\). The walls of the veins are always thinner and more supple than those of the arteries\(^6\), and lymphatic vessels have thinner walls than their venous counterparts\(^6\).

For example, the primitive lymph ducts are phylogenetically-paired right and left vessels with various prevertebral cross-communications between the right and left vessels; one such communication lying on the plane between the posterior and superior mediastinum, and therefore not subject to pressure by the aorta, is enlarged\(^1\).

**Gross anatomy**

(1) The branches of the aortic arch, including the brachiocephalic trunk, common carotid artery (and its branches), subclavian artery and axillary artery, run deep to the brachiocephalic veins and their tributaries to more directly reach their targets, though the aortic arch is superficial to the superior vena cava.

Because the bilateral external iliac arteries run forwards and downwards, the distal part of the abdominal aorta and its branches, including the common iliac artery, external iliac artery, and the proximal part of the internal iliac artery, run superficial to their corresponding veins, even though the upper part of the abdominal aorta is deep relative to the corresponding part of the inferior vena cava. The distal part of the internal iliac artery runs backwards, and is deep relative to its vein.

(2) The subclavian artery and the brachial plexus pass through the scalene space and run laterally and downwards, together with the subclavian vein, while the subclavian artery is pushed medially and inferiorly by the brachial plexus. The scalene space only has room for the brachial plexus and subclavian artery, and the subclavian vein has competitively pushed in front of the anterior scalene muscle.

(3) The brachial plexus travels with the axillary artery to enter the axilla. The plexus emerges from the cervical portion of the vertebral column and the great artery arises almost directly from the heart. The plexus would thus be predicted to lie above, behind, and then lateral to the artery, as observed. The three cords of the plexus are disposed around the second part of the axillary artery (the part behind the pectoralis) as their names suggest, serving their targets; the plexus has the more direct
position relative to the artery.

(4) Considering the brachial and ulnar arteries (its continuation) as the great arterial stem of the upper limb, this arterial stem curves laterally, pulled by the radial artery at the elbow, whereas the median nerve pursues a straight course. Given that the elbow joint is always flexed in the embryo, the median nerve takes the shortest route, crossing superficial to the brachial artery in the arm and to the ulnar artery in the forearm.

(5) Regarding the fibrous digital sheath, the palmar nerves lie anterior to their fellow arteries.

(6) Several pelvic nerves, arteries, and veins pass through the suprapiriform and infrapiriform foraments on the dorsal wall of the pelvis and enter the gluteal region, which is dorsal and lateral to the pelvis. Most of the nerves and blood vessels are arranged laterally to medially, respectively, and the larger the nerve, the more lateral it lies. As all the nerves emanate from the midline of the body, more lateral means more direct to the gluteal region. The pudendal nerve and the internal pudendal artery and vein are arranged medially to laterally, respectively[1], because their targets are medial to the foramen.

(7) The external iliac artery becomes the femoral artery midway between the symphysis pubis and the anterior superior iliac spine, and passes through the femoral triangle. In the triangle, the femoral artery runs along a boundary line that separates two independent motor-nerve territories. The femoral nerve supplies the muscles of the lateral territory[1]. It enters the triangle slightly lateral to the artery, while the femoral vein lies medial to the artery, and the deep lymph vessels lie mainly medial to the vein[1]. In this case, the nerve and artery both take their own most direct route, following the vein and lymphatic vessels, respectively.

(8) The tibial nerve can be considered as the great nerve stem, and the femoral, popliteal, and posterior tibial blood vessels as the great blood vessel stem of the lower limb. The great nerve stem pursues a straight course down the back of the limb, while the great blood vessel stem descends at the front of the limb, runs laterally and dorsally, and enters the popliteal fossa from the medial side. The vessels are therefore initially medial to the nerve, which enters the fossa from the upper angle of the fossa. The artery takes the more direct route lying before the vein at the apex of the femoral triangle, and medially and ventrally to the vein at the popliteal fossa. The great blood vessel stem then curves laterally, pulled by the anterior tibial peroneal blood vessels, before resuming its course medially. The nerve, however, continues on a straight course. Because the knee joint is always flexed in the embryo, the nerve takes the shortest route, passing superficial to the great venous stem.

(9) The posterior tibial artery and tibial nerve are each divided into medial and lateral plantar branches at the ankle. These nerves and arteries adjust their positions, with the arteries passing superficial to the nerves[1], such that the nerves take the shortest route into the sole of the foot.

(10) The intercostal nerves, posterior intercostal veins, and posterior intercostal arteries[1] cross the corresponding intercostal space obliquely towards the angle of the upper rib, and then continue forward in the costal groove, where they are protected from pressure during the action of the intercostal muscles. Each posterior intercostal artery is accompanied by a vein and a nerve, above and below the artery, respectively. The nerve adopts the most direct route to their targets, the intercostal muscles, followed by the artery, and then the vein.

(11) The facial artery takes a deeper and more anterior course than the facial vein in order to send branches to the lips and nose, and then run to the medial angle of the eye.

(12) The suprascapular nerve runs laterally and downward to the supraspinous fossa beneath the superior transverse ligament of the scapula, while its accompanying artery passes over the ligament.

(13) The internal thoracic artery always lies lateral to the internal thoracic vein to more directly supply the intercostal space.

(14) The nerve, artery and vein in the obturator canal are arranged from above downwards.

Supplementary explanations

(1) Lymph vessels are more slender than their accompanying great blood vessels or nerves. When lymph vessels travel together with these great structures (such as in the femoral triangle), most will follow the same principles and adopt a less direct route than the great veins, whilst being as direct as possible. Although a few of them may pass through the space around these great structures, they also apply the principle "as direct
as possible”.

(2) Although middle-sized arteries are closely accompanied by paired veins, one on each side, the two veins still take less direct routes than their artery.

(3) Visceral efferent fibers are thin, myelinated or unmyelinated fibers. Autonomic nerves often run along the arteries and form a plexus around them, otherwise they could be ruptured by even slight shaking. These nerve fibers thus travel with their arteries on the same direct route.

(4) When other stronger structures encounter nerves or vessels, the stronger structures adopt the most direct position. Tendons are stronger than nerves or vessels, and the tendon of the extensor hallucis longus is positioned in front of them at the bend of the ankle. The principal bronchi are stronger than blood vessels, and the largest part of the lungs is behind the hilum. The bronchi therefore inhabit the posterior part of the hilum, dorsal to the great vessels. For the same reason, the renal pelvis inhabits the posterior part of the renal hilum; and the right and left hepatic ducts inhabit the anterior part of the hepatic hilum.

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