The Primo Vascular System: A Unique Human Biological System Shifting Medical Paradigm

Prospective Osteopathic Applications for Cranial, Visceral, Lymphatic, and Fascial Techniques

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Highlights

- The primovascular system (PVS) is a rediscovered morphodynamic system initially described in 1961.
- Using state of the art technology, a scientific team reinitiated the PVS research in 2002 confirming its existence in many structures of the central and peripheral nervous systems, on the surface of most viscera, in lymph and blood vessels, as well as in adipose tissue.
- The PVS carries a high concentration of nucleic acids and adult small embryonic-like stem cells as well as hormones in secretory granules.
- The PVS has circulatory properties, endocrine functions, supports anti-inflammatory processes and may be a new player in the physiopathology and treatment of cancer.
- The PVS system may have interesting implications for osteopathic manual medicine. The presence of “primo-vessels” in several vessels and nerves, viscera and fascia, and in the brain and spinal cord could potentially open novel possibilities of integration for cranial, lymphatic, visceral and fascial approaches in osteopathic manipulative treatment.

Keywords:

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Lymph
Lymph Drainage Therapy
Lymphatic System
Manual Therapy
Manual Lymphatic Therapy
Osteopathy
Osteopathic Lymphatic Technique
Osteopathic Manipulation
Osteopathic Manipulative Medicine
Palpation
Primo-vascular System

Abbreviations/Acronyms:

BHD: Bong-Han Duct
BHK: Bong-Han Kim
BHS: Bong-Han System
LDT: Lymph Drainage Therapy
MLDT: Manual Lymph Drainage Therapy
MT: Manual Therapy
OLT: Osteopathic Lymphatic Technique
OMM: Osteopathic Manual Medicine
PF: Primo-vascular fluid or Primo-fluid
PN: Primo-vascular nodes or Primo-nodes
PV: Primo-vascular vessels or Primo-vessels
PVS: Primo-Vascular System

Abstract

This article describes the historical background and pathophysiologic aspects of the Primo-Vascular System (PVS). The PVS is depicted as being the most recent body system to be discovered, with a specific anatomical and immunohistochemical signature that sets it apart from the arteriovenous and lymphatic systems. It is comprised of immune functions, endocrine functions, and is found to be deeply involved in several biological processes, including tissue regeneration, inflammation and cancer.

Though ongoing research has been conducted since 2002, the original discovery was actually made in the 1960's by Bong-Han Kim, a North Korean scientist, which went virtually unnoticed for a span of nearly 40 years.

The presence of “primo-vessels” in and around several vessels and nerves, viscera and fascia, and in the brain and spinal cord, reveals a common link that could potentially open novel possibilities of integration for cranial, lymphatic, visceral and fascial approaches in osteopathic manual medicine.

Introduction

Even in an age where a profuse amount of scientific data is revealed on a daily basis, it is rare to suggest the existence of another human body system. A novel circulatory system was first described by Bong-Han Kim as the "Substance of Kyungrak" in the 1960’s. Advanced evaluation methods later confirmed this system as the Primo Vascular System (PVS) and its existence in multiple anatomical structures in animals and the human body.

A relatively recent body system like the lymphatic system was officially discovered as far back as 1627 [1]. The PVS being the latest candidate to the list of human body system, thought formally described in 1961-1962, was not scientifically authenticated until 2002.

This literature review article presents the past and the present research on the Primo-Vascular system, and describes its historical background and physiologic aspects as well as the current state of understanding on PVS.

The presence of the PVS, if fully confirmed, suggests possible implications that may fundamentally reshape our vision of anatomy, physiology and medicine, consequently impacting osteopathic manipulative medicine and manual therapy.

Discovery of the PVS

There are two distinct eras of discovery and research of the PVS occurring nearly 40 years apart.

A. Initial discovery: from 1961 to 1965

Bong-Han Kim (1916-?), professor at the Pyongyang Medical School in North Korea, embarked on scientific research to discover the substratum for the acupuncture meridians. While head of the department of physiology in Pyongyang, Bong-Han Kim made his initial announcement about the anatomical substratum for the acupuncture meridian system (“Kyungrak” in Korean), called "Substance of Kyungrak", on August 18,

1961, which he then published in 1962 [2].
In 1962, he wrote in his manuscript that the acupuncture meridian system "*consists of bundles of tubular structures and it is clearly distinguishable from nervous, blood vessels and lymph systems in histological and experimental-biological characters*." [2] and *"the diameter of the tubular structures range between 20 and 50 microns."* [2].
Bong-Han Kim subsequently published five detailed articles about his research from 1962 to 1965 [3-8].
He used histological techniques (Hematoxylin and Eosin, Mason's trichrome, Verhoff, silver staining, Feulgen reaction, Acridine orange), radioactive tracers, and electrophysiological methods. He identified the PVS using a specific blue dye, unfortunately his reports lack full scientific descriptions of his materials, methods, and protocols, which proved highly challenging for researchers of the time wanting to confirm his findings.

One of Bong-Han's reports were translated into English and made readily available for research teams [7], which led numerous groups in China, Japan, and Russia to try to confirm his findings [9]. Fujiwara and Yu, in Japan, were able to partially reproduce Kim's findings inside blood vessels, and on the surfaces of viscera [10] , and some Chinese teams may have also reproduced some of Bong-Han Kim's results in rabbits [11] , however, one of the main reasons that scientific teams could not properly reproduce his results was that the specific blue dye that Bong-Han used to make the system visible and conduct his research, was never fully described. The scientific community of the time eventually abandoned the idea of a definite Bong-Han system of ducts and nodes.
Around 1965, the institute in North Korea, where Bong-Han Kim was working, unexpectedly closed. The Bong-Han theory has been largely forgotten for about four decades, and to this day Bong-Han Kim's fate is unknown [12].

Table 1: Reported discoveries of Bong-Han Kim.

Reported Discoveries of Bong-Han Kim

- Bong-Han Kim (BHK) claimed he discovered a new circulatory system inside plants, invertebrate, and mammals, especially rabbits. He said this was the "Kyungrak System", meaning the system of "acupuncture meridians and collaterals" in Korean.
- The so called Kyungrak system (or Bong-Han/BH system) consisted of a network of Bong-Han ducts (or BH ducts), Bong-Han corpuscles (or BH corpuscles), and Bong-Han liquor (or BH liquor), circulating inside of them, a liquid high in chromatin.
- Bong-Han Kim, using radiotracer, described the BH ducts as being comprised of many smaller ductules composed of endothelial cells with characteristic rod-shaped nuclei.
- He applied biochemical and histochemical analyses of the BH system and found that the fluid inside the ducts is transparent, and contains more nucleic acids, especially DNA, than any other tissue.
- He described the components of the BH liquor as:
- Total nitrogen content: 3.12–3.40%
- Non protein nitrogen content: 0.10–0.17%
- Lipids: 0.57–1.00%
- Reduced sugar: 0.10–0.12%
- Total hyaluronic acid: 170.4mg%
- More than 19 free amino acids
- More than 16 free mononucleotides
- Very abundant DNA and RNA nucleotides

- For Bong-Han Kim, the BH ducts also contain “sanals“, meaning “live egg” in Korean which seems to have a function equivalent to that of stem cells. Bong-Han Kim described these “sanals”, modernly renamed Primo-microcell or P-microcell, as having hematopoietic functions, and being able to regenerate injured tissues, and heal wounds.
- BHK described 5 sub-systems (BHS = Bong-Han System):

1. The intravascular BHS: located inside the blood vessels, the heart and the lymphatic vessels.
2. The organ surface BHS: freely floating on the surfaces of viscera.
3. The extravascular BHS: running along the blood and lymphatic vessels, as well as the nerves. It is located just outside of these structures.
4. The nervous BHS: located inside the central and peripheral nervous systems, floating in the cerebrospinal fluid.
5. The intra-organ BHS: located inside visceral parenchyma.

- Electrical conductivity of a Bong-Han vessel recorded by Bong-Han Kim:
Bong-Han Kim identified three periodic potentials of 15-30 seconds, 7-10 seconds, and 20-25 seconds. The method used to measure these signals was not specifically described.
- According to the research of Bong-Han Kim, damage to Bong-Han vessels can “modify the frequency and amplitude of the heart and change the peristaltic motion of intestines.” It can also reduce nerve excitability and decrease muscular contractions.

B. Scientific Confirmation: from 2002 to the Present Time

Around 2000, Kwang-Sup Soh, professor in the Department of Physics at the Seoul National University (1976–2011) also formed a Biomedical Physics Laboratory to examine the scientific reality of the acupuncture meridians. He chose Dr. BC Lee as the main researcher to reexamine the findings of Bong-Han Kim using the latest technology available.
After a series of trials and errors they finally observed Bong-Han ducts floating on the surfaces of rabbit viscera, such as the liver, the stomach, the intestines and the bladder [13].
In 2002 Kwang-Sup Soh proposed a change to the terminology specifically changing the name “Bong-Han system” to “Primo-vascular system” (see Table 2). This change was later endorsed by the 2010 International Symposium on the Primo Vascular System [14].

Table 2: Primo Vascular System Terminology.

Primo Vascular System Terminology

Terminology changes of Kwang-Sup Soh (2002/2010)

- Bong-Han system (initially called the “Kyungrak” system) was changed to Primo-vascular system (or PVS)
- Bong-Han duct was changed to Primo-vessel or Primo-vascular vessels (or PV)
- Bong-Han corpuscle was changed to Primo-node (or P-node)
- Bong-Han liquid was changed to Primo-fluid (or P-fluid)
- Bong-Han “Sanal” was changed to Primo-microcell (or P-cell)

In 2008, Dr. BC Lee of the Soh group and his team discovered a dye that can be sued in a specific manner to identify the PVS: Trypan blue [15].

From there, the Seoul National University (SNU) could observe the PVS in the bovine heart, the brain ventricles, and in the central canal of spinal cords, as well as, for the first time, in the abdominal adipose tissues.
In 2011, Prof. K.S. Soh's team of the Seoul National University Department of Physics formed the Nano Primo Research Center of SNU's Advanced Institute of Convergence Technology, where he would head the research.

Identification of the PVS

To visualize the PVS, a great deal of advanced technology has been used [16], including confocal laser scanning microscopy [17], scanning electron microscopy (SEM), cryo-SEM, focused-ion-beam SEM, high voltage transmission electron microscopy (TEM) [18], electron microscopy (for the surfaces of mammalian organs) [18, 19] ; atomic force microscopy [20]; fluorescent nanoparticle [21]; immunohistochemistry [22, 23]; proteomic analysis [24]; and the ELISA technique for the primo-fluid content [25, 26].
Before the discovery of Trypan blue [27], Janus green [28] and Alcian blue dyeing [29] were used with moderate success to identify the PVS.
Trypan blue is not a specific marker of PVS. Trypan blue has been widely used in the analysis of cell cultures to stain dead or dying cells in culture and as early as the 1930's this dye was known to stain damaged or inflamed tissue (e.g. Menkin V. 1931) 30. Trypan blue also has been used to stain lymphatic vessels (e.g., Leak LV et al. 1978) 31, and Li H and Li J. (2003) 32. To identify the PVS, Soh's team used subjects in a non pathological state and the method for detecting PVS requires specific procedures that were developed in the Nano Primo Research Center. If this procedure is not followed the PVS sample is not detectable (Prof. Soh KS, personal communication).

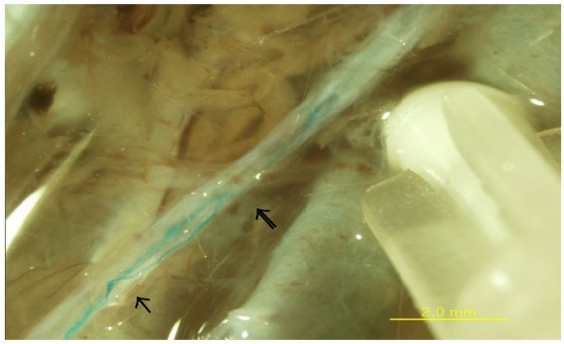

Image # 1

Stereomicroscopic in situ image of a branched and rejoined primo vascular system (blue stain) in the thoracic duct of a subject rat. Two regions of branching (arrows) and rejoining (open arrows) are observed.
In Kim S, Jung SJ, Cho SY, et al. A Method for the Observation of the Primo Vascular System in the Thoracic Duct of a Rat. Evid Based Complement Alternat Med 2013; 2013: 5.
http://dx.doi.org/10.1155/2013/536560.
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Anatomical Overview of the PVS

The primo-vascular vessels have been identified in rabbits as thin semitransparent structures of an average

diameter of approximately 20 to 30 μm [19, 33, 34]. Each vessel contains several, (up to 20), smaller ductules, 3–10 μm in diameter that are lined by a single layer of endothelial cells and surrounded by extracellular matrix (ECM) [34]. Each ductule is filled with a liquid called primo-fluid [18, 19, 34]. They can be connected to primo-vascular nodes (PN) [35].

Nowadays, primo-vessels are fairly easily differentiated from blood vessels, and they present many differences with lymph vessels. Primo-vessels are not lymphatic, nor blood vessels, as they don't express LYVE-1 (specific lymphatic endothelial marker, a CD44 homolog), nor CD31 (blood vessel specific marker). The rod-shaped nuclei of the PVS endothelium cells are aligned parallel to the wall of the primo-vessels, and can be specifically stained by Acridine orange, fluorescent phalloidin (F-actin), or DAPI [9, 27, 33, 36-38] . Rod-shaped nuclei are hall marks of the PVS, regardless of which animals or organs the PVS was taken from. One problem is that the rod-shaped nuclei can easily be seen and identified in longitudinal views, but are very difficult to see or identify in cross section images.

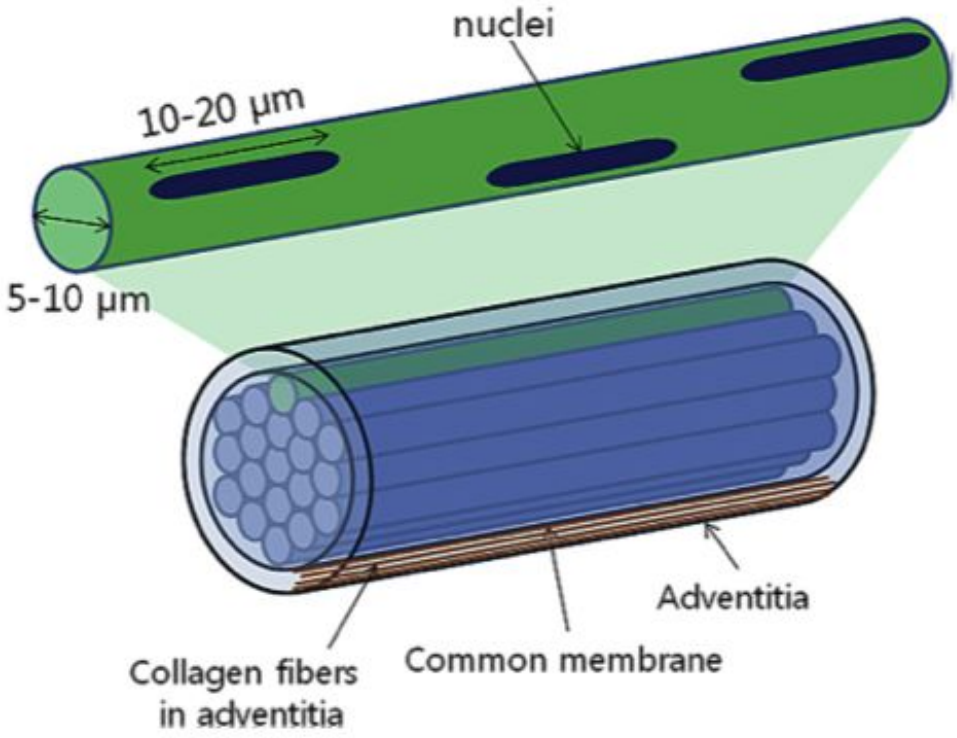

Image # 2

Illustration of one isolated subvessel (top) and a bundle of subvessels of the primo vessel.

In Stefanov M, Potroz M, Kim J, et al. The Primo Vascular System as a New Anatomical System. J Acupunct Meridian Stud 2013; 6(6): 331-8. http://www.ncbi.nlm.nih.gov/pubmed/24290797.

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Composition of the Primo-fluid

The composition of the primo-fluid of rats has been found to be rich in granulocytes and secretory granules: mast cells (20%), histiocytes (53%), eosinophils (16%), neutrophils (5%), round immature stem-like cells (3%), and relatively poor in lymphocytes (1%) [39].
In the PVS, researchers measured a high concentration of adult small embryonic-like stem cells (very small embryonic-like stem cells) expressing the stem cell biomarkers oct4, nanog, and CD133 [34, 39, 40].

Location of the Primo-Vascular System

i. Heart

Inside the bovine heart [41], on top of bovine endocardium [42], Lee et al. visualized a complex arrangement of endocardial vessels (20 μm in thickness).

ii. Blood Vessels

Primo-vessels has been identified inside large blood vessels [43-47]. In particular, primo-vessels have been identified floating inside the abdominal artery and the caudal vena cava of rabbits [48], rats [49], and mice [46].
PVS has also been discovered in the superior sagittal sinus of a rabbit brain [50].

iii. Lymphatics

PVS were detected within lymphatic vessels [28]. The primo vessels inside the lymphatic vessels can often be visible in transparency, with no contrast agent, from outside the vessel, as lymph vessels are quite transparent [36, 51-53]. PVS have also been isolated floating inside lymph vessels using Alcian blue [53], and fluorescent nanoparticles [36].

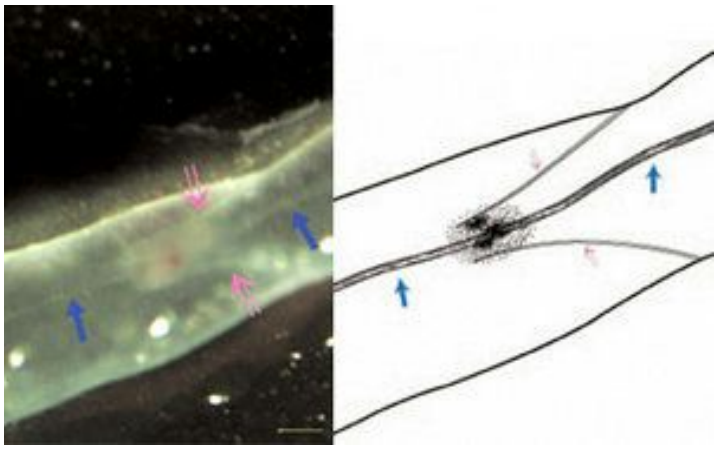

Image #3

Presence of a primo vessel within the lymphatic vessel of a rat.
In Johng HM, Yoo JS, Yoon TJ, et al. Use of magnetic nanoparticles to visualize threadlike structures inside lymphatic vessels of rats. Evid Based Complement Alternat Med 2007; 4(1): 77-82. http://www.ncbi.nlm.nih.gov/pubmed/17342244/.
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iv. Central Nervous System

The PVS was found inside the venous sinuses of rat brains, [54] and also emerged in the circulatory system.
In the CSF, primo-vessels were found running within the central canal of the spinal cord by using fluorescent nanoparticles that were injected into the lateral ventricles [21], and underneath the superior sagittal sinus in the sagittal fissure of rabbits, where its characteristics were the same as those observed in other organs [50].

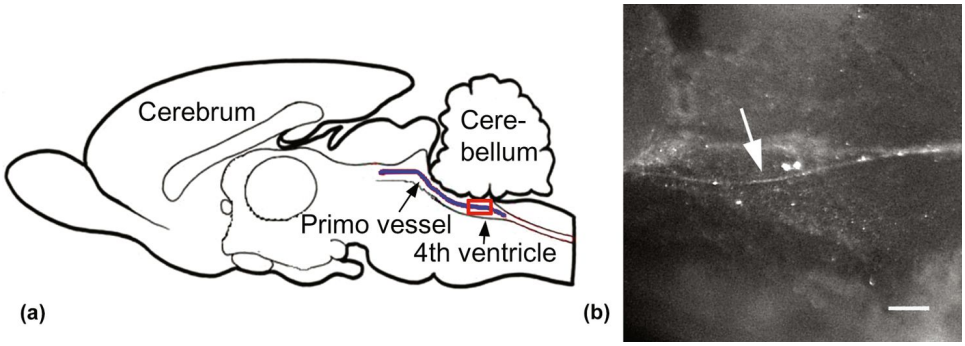

Image #4
Primo-vessel floating inside the ventricular system of the brain.
In Lim J, Jung JH, Lee S, et al. Estimating the density of fluorescent nanoparticles in the primo vessels in the fourth ventricle and the spinal cord of a rat. J Biomed Opt 2011; 16(11): 116010-7.
http://www.ncbi.nlm.nih.gov/pubmed/22112115.
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v. Peripheral Nervous System

PVS has been located around the perineurium of the spinal cord, and in the epineurium, perineurium, and endoneurium, of rat sciatic nerves [27].

vi. Viscera

Primo-vessels have also been identified on the surface of numerous viscera, such as the stomach, intestines, liver, bladder, and heart [19, 23, 25, 41, 55]. They have also been identified floating in peritoneal fluid [17], in the omentum, and in the peritoneum [15].

vii. Skin and Adipose Tissue:

Examples of PVS can be found in the hypodermis of rats by using Trypan blue [56, 57], in the adipose tissues [58], and in the rat hypodermis, primo-vessels could be found by using fluorescent nanoparticles [57].

Electrophysiological Measurements of the PVS

Different excitable nerve-like structures have been found in the PVS, which express spontaneous electrical activity [59, 60]. Electrical recordings of the internal organs identified two different types of pulses produced by the PVS, with irregular electrical bursts of spontaneously activity, that can be either transversal or longitudinal, and that can be easily differentiated by neighboring smooth muscle contractions [61, 62].
The contractility of the PVS is slowed down by activation of acetylcholine muscarinic receptors and modified by nifedipine, suggesting the presence of voltage-dependent Ca^{2+} channels in primo-vessels [62, 63].

Embryology

According to experiments with chicken eggs, the apparition of the PVS precede the formation of the extra-embryonic vessels, embryonic arteries, veins, and lymphatic vessels, as well as nerves, and viscera [64].

Presence of PVS

i. In Humans

Recent human data on the PVS has been published by Lee et al. [65]. The PVS in humans was found inside the live blood vessels of the umbilical cord (UC) of a placenta. The PVS was observed both on the fascia and inside the blood vessels of the UC. Surprisingly, human primo-vessels were no thicker than those of small animals.

ii. In Animals

Bong-Han Kim primarily used rabbits for his experiments on the PVS, but affirmed that he had identified the PVS in hydra, fish, amphibians, birds, and numerous mammals, including humans [4]. Since 2002 the PVS has been located in mice, rats, rabbits, dogs, pigs, and cows.

Functions of the PVS

i. Circulatory Functions/Transport

The PVS circulates in a network of vessels and nodes with multiple independent paths that can stay connected. The entire PVS network has yet to be fully mapped in humans. The speed of the primo-flow was measured at approximately 0.3 ± 0.1 mm/second in rabbits, using Alcian blue [19], and at around 100-800 m/second with direct measurement using fluorescent nanoparticles [19, 66, 67].

Within the primo-fluid, the circulatory nature of the PVS can help transport chemical substances, factors of inflammation, possibly medication, as well as cancer cells (metastases), in pathological processes. The PVS has been foreseen as a potentially novel drug delivery route, particularly for cancer treatment [68].

i. Immune and Regenerative Functions

Primo-fluid contains a high concentration of very small embryonic-like stem cells, approximately 1-4 m in diameter, whose exact function still needs to be determined [40, 69].

A research team led by BS Kwon, at the National Cancer Center of Korea, [39] confirmed that the PVS was abundant with other immune cells, such as macrophages, eosinophils, and mast cells [18].

ii. Endocrine Functions: Neurotransmitter Pathway

The PVS has also been described as an endocrine organ which transports different hormones [25, 26, 70]. Catecholamines (adrenalin and noradrenalin) have been identified in the primo-fluid of the organ surface of rabbits and rats with the ELISA technique [25, 39].

iii. Bioluminescence (Biophotons)

Popp et al. described different types of biophoton emissions within living systems [71, 73].

The PVS contains a high concentration of nucleic acids, and is surrounded by collagen. Consequently, Lee and Soh suggested that the PVS can be a good medium to transport, or communicate, tissue bioluminescence (biophoton) [53, 68].

Role of PVS in Pathology

i. Inflammatory Process

Wang et al. in China showed that the PVS of infected rats carries pathological products, which may be involved in inflammatory processes [73].

ii. Cancer

In mammals, the PVS has been identified on the fascia surrounding tumor tissue, or connected to tumors [9, 74, 75]. The PVS may be a newly recognized player in cancer growth control, and may potentially be a novel path for cancer metastasis, as primo-vessels are more concentrated around tumor sites, and migration of tumor cells is more efficient inside the PVS than in the lymphatic system [74-77].

Applications for Osteopathic Manual Medicine: Potential Integration of Cranial, Lymphatic, Visceral and Fascia Approaches

G.W. Sutherland (1873-1954), that may have continued the legacy of Swedenborg(1688-1772) [78]., described the “potency” of the cerebrospinal fluid, calling it the “fluid within the fluid”, and again toward the end of his life he described it as a “liquid light” [79].

It would be interesting to debate, whether or not, Sutherland’s descriptions of a “fluid within the fluid” and of a “liquid light”, might potentially be actual early descriptions of some aspects of the yet unknown primo-vascular system.

Primo vessels are ubiquitous channels for transporting fluid with immune and endocrine functions.
Initially, primo-vessels could, for example, be accessed manually through the lymphatic vessels using specialized osteopathic lymphatic techniques. Furthermore, like for most structures of the body, primo-vessels specific motilities could be looked for (this remains to be confirmed by further research).
The PVS could reasonably link tissue functions across "systems". The PVS plays intriguing roles in tissue where osteopathic manipulation has distinct efficacy, including fascia, membrane, lymph, viscera, nerve and central nervous system. Since osteopathic manipulation can benefit vasculature, lymph, and capillary flow, it is reasonable to suggest that this additional fluid system can also be affected which would both positively influence, and further expand, the scope of osteopathic practice.

Discussion

The work of the Soh group is undoubtedly intriguing and would need to be confirmed by a number of other scientific teams. Circulatory aspects of the PVS have been described, Kim BH showed three periodic potentials of 15-30 seconds, 7-10 seconds, and 20-25 seconds, for the PVS but he did not describe a pulsatory type measurement. It remains a challenge to measure such rhythmic aspects in the human body. Further research evaluating the physiological importance and circulatory effects of the PVS is required and eagerly awaited. Future endeavors may hopefully reveal more convincing evidence and substantiate a rhythmic aspect of this novel circulatory system, and its potential palpation by trained osteopaths, as the PVS is on the surface of many organs and in the subcutaneous layer.
If the anatomy and pathophysiology of the PVS, in particular its applications to inflammation, endocrinology, and oncology are confirmed, it will expand our understanding of the human body systems and will create a general paradigm change in medicine.

Conclusion

It is difficult to fathom that the prolific Primo-Vascular System was not identified in medicine until recently. Both Bong-Han Kim and Kwang-Sup Soh initially targeted their research at discovering the meridian system of acupuncture, but found something more surprising and far reaching. The discovery of the PVS in intravascular and extravascular spaces, in the central and peripheral nervous systems, on the surface of and within viscera, in cutaneous layers, and in most body systems, may signify a novel and complete morphodynamic system, with potential to reshape paradigms in medicine and osteopathic manipulative treatment.

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Author's Contribution

The authors contributed equally to this work.

Disclosure Statement

The three authors have no direct or indirect financial interests.

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