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PROGRESSION OF INTRA-CEREBRAL HEMORRHAGIC STROKE

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DISCLAIMERS:

1. The theory presented in this draft paper did not go through a standard peer review. It presents propositions about some physical hydraulic-based phenomena occurring during hemorrhagic strokes.
2. Medical recommendations presented at the end of the paper are speculative and must go through a rigorous theoretical and experimental analysis.

Key Proposition*: Intra-Cerebral* **arterial** hemorrhagic stroke causes a catastrophic collapse of the blood vessels and capillaries on the venous side of the brain's blood circulatory system and rapidly retards the blood flow ***across the entire brain***.

1. ABSTRACT

The paper's theoretical analysis rests on postulating a co-existence of ***two separate pressure domains*** within the cardiovascular system: arterial domain and venous domain. The paper suggests that a large difference between the blood pressure in these domains significantly impacts to the initiation, progression, and consequences of hemorrhagic strokes.

Progression and consequences of Intra-Cerebral Hemorrhage Stroke (ICHS) are defined, and strongly influenced by the location of the hemorrhage in the brain and depend, crucially, on whether the ICHS occurs on the arterial or, significantly less often, on the venous side of the brain blood circulatory system.

In this paper, progression of an ICH stroke caused by rupture of an arterial blood vessel due to hypertension is addressed based on an analysis of the hydrodynamic processes taking place in the brain blood circulatory system during the stroke. This analysis of ICH stroke considers the transitory events in the arterial and venous branches of the blood vessel network which may lead to rapid and catastrophic deterioration of the blood supply to multiple areas throughout the brain.

(The ICHS development in time may have autocatalytic features where initial vessel collapse is intensified by its effects, acting as feedback accelerating ICHS progresses. This assumption, if correct will require confirmation by lab experiments.)

Intra-cerebral hemorrhage, as opposed to ischemic stroke, may lead to **global** brain damage in all regions of the brain supplied by blood through the arterioles, capillaries and the so-called perforators. The rate and progression of development and magnitude of the damage will depend on the size of the rupture. The blood flow retardation starts on the venous side due to collapse of veins, sinuses, venules and capillaries (all being low blood pressure vessels) and then progresses to the cerebral arteries and arterioles due to flow stagnation on the venous side. This global collapse of the circulatory system develops rapidly until a quasi-steady state is reached. Ischemic strokes (IS), on the other hand, lead to a slower developing, much more localized damage predominantly in the brain regions immediately downstream of the vessel blockage resulting in consequences that are less severe than those of ICHS[1]. It must be added that ICHS, in addition to global effects will also produce localized effects in the vicinity and downstream of the rupture similarly to IS.

One of the major symptoms of ICHS is a rapid partial or total loss of consciousness indicating a massive shock to multiple areas of the brain. On the other hand, in ischemic stroke, "…deficits may become maximal within several minutes of onset, typically in embolic stroke. Less often, deficits evolve slowly, usually over 24 to 48 h (called evolving stroke or stroke in evolution), typically in thrombotic stroke. In most evolving strokes, unilateral neurologic dysfunction (often beginning in one arm, then spreading ipsilaterally) extends without causing headache, pain, or fever. Progression is usually stepwise and may be interrupted by periods of stability." [2]

Accurate mechanistic analysis of the progression of ICHS taking into account the hydro-mechanical effects of the event should offer a better understanding of stroke progression and, consequently, may offer a path to the development of more effective treatment of its consequences.

2. DEVELOPMENT AND PROGRESSION OF ARTERIAL HEMORRHAGIC STROKE

In the schematic of the blood circulatory system shown below[3], the blood flows from left to right entering the brain region through the arteries, propagating through the arterioles and capillary networks, and leaving through the venules and veins.

There are two self-contained pressure regions in the brain that normally are hydraulically disconnected. One such region is the entire network of cerebral blood vessels enclosing the continuously circulating blood. This is a "high" pressure region where the static blood pressure oscillates with the heart beat from the systolic (around 115 mm of Hg relative to atmospheric pressure) to diastolic (around 75 mm of Hg) pressure level on the arterial side (left part of the illustration below) and stays almost constant at around 5-8 mm of Hg on the venous side (right part of the illustration). "Pressurized blood within this region is isolated (both in terms of direct flow and pressure transfer) from the second self-contained "low" pressure region of the brain by the mechanical stress inside of the blood vessel walls. This low pressure region is the brain's interstitial region where the pressure is significantly lower than in the high pressure region and is close to atmospheric pressure.

[1] Literature search is underway

[2] MERCK Co. publication (**http://www.merck.com/mmpe/sec16/ch211/ch211b.html**)

[3] *My Stroke of Insight, A Brain Scientist's Personal Journey,* Jill Bolte Taylor, VIKING, 2006 *(some notations have been added to the schematic by the author)*

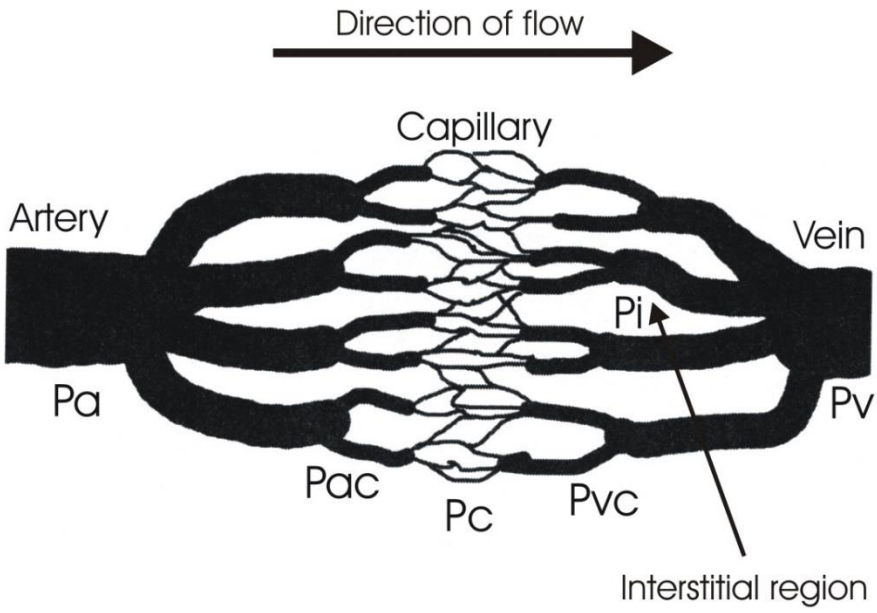

Fig.1
The notations in the schematic are as follows:
Pa – arterial pressure,
Pv – venous pressure,
Pc – pressure in capillaries,
Pac – pressure in arterioles,
Pvc – pressure in venules,
Pi – pressure in the interstitial region of the brain.

The variation of blood pressure in different regions of the blood circulatory system starting from the high pressure region (artery) to the low pressure region (brain interstitial region) can be expressed as follows:

$$Pa > Pac > Pc > Pvc > Pv > Pi.$$

Consequently, immediately following a rupture of the artery, pressure in the interstitial region of the brain will increase and rapidly approach the arterial pressure since the intra-cranial region of the skull has very limited capability to dampen the pressure shock induced by the rapture. Thus, the intra-cranial pressure, Pi, will increase rapidly from near atmospheric to close to arterial pressure, Pa. Since the difference in pressures between the arterial and venous sides is very large, up to 110 mm of Hg, the entire venous blood circulatory system (5 to 8 Hg mm pressure vessels) including the capillaries located between the arterial and the venous systems (central part of the illustration) will quickly implode thus preventing or significantly hampering the blood circulation through the brain[4]. This will lead to brain damage in multiple regions throughout the entire brain (global effect) unlike the case of ischemic stroke where only the brain regions lying downstream of the vessel blockage are directly affected (local effect).

The process described above will develop in rapid progression: initial reduction of venous flow due to collapse of the smaller size venules and capillaries (no blood is able to leave the brain region) leads to increase in interstitial pressure, Pi, which, in turn leads to collapse of the larger and larger venules, veins, and sinuses until a quasi-steady state condition is reached with the blood circulation severely retarded.

The following components of damage to the brain can be suggested. First, the brain tissue will starve of oxygen and glucose caused by a severe retardation of the blood circulation. Second, parts of the brain will undergo local

[4] Depending on the size of the particular blood vessels and the thickness and structure of their walls, their collapse may not be complete, allowing for some blood flow to continue following ICHS.

structural mechanical deformation in the immediate vicinity of the vessel rupture where the brain tissue will be displaced by the forming blood clot and in the vicinity of the collapsed veins; this process will continue until the bleeding stops and the blood clot stops growing. Third, there will be structural brain damage due to development of a brief "outflow" of the brain tissue through the vertebral canal and other skull penetrations (see insert below) caused by the elevated intracranial pressure. Finally, damage to the nervous system may develop when the nerve cords (hearing/visual, spine) in the vicinity of the skull penetrations *[NOTE: must use appropriate medical terminology when referring to the cords and penetrations]* are deformed by the outflowing brain tissue. The hydro-mechanical phenomena presented above will be investigated in the laboratory experimental investigations and through numerical modeling.

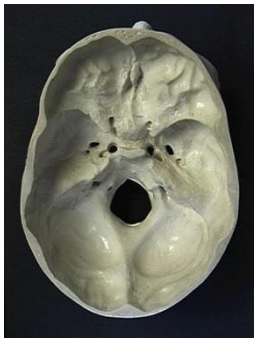

Fig. 2

3. EXPERIMENTAL INVESTIGATION OF ICH STROKE PROGRESSION

A physical experimental laboratory hydro-mechanical model of the brain circulatory system including the brain interstitial region is being presently designed. The ICHS stroke scenario experiments measuring and recording pressures as a function of time in all areas of the model will be conducted under (a) static pressure boundary conditions (constant Pa and Pv) during the simulated arterial rapture and (b) oscillating pressure boundary conditions approximating a real case situation. Pressure measurements in all six model areas (Pa, Pac, Pc, Pvc, Pv, and Pi) will be performed starting from the inception of the simulated arterial vessel rupture until the steady state or quasi-steady state conditions are reached.

The same experimental model can also be used to investigate the progression of IS or to model the processes developing in the venous hemorrhage scenario.

4. MEDICAL DATA SEARCH

Literature search on ICHS and IS their specifics symptomatic features, including their temporal and spacial progression and consequences must be conducted and the comparative analysis performed. TBD

5. CLINICAL APPLICATION

The clinical application of the proposed analysis of ICHS development and consequences lies in diagnosis and post-stroke treatment of patients suffering stroke due to ruptures of blood vessels in the brain.

By far, the most challenging are ruptures of blood vessels located in the arterial leg of the brain blood circulatory system that may lead to global catastrophic damages to the brain.

Ruptures of vessels on the venous side of the brain blood circulatory system occur significantly less often, have consequences expressed in smaller, localized areas, and lead to brain damages only in limited areas, producing symptoms closer to those of the ischemic strokes, IS.

The preventive and post-stroke treatment of the patients may differ between these types of vessel ruptures. Results of the proposed research may be useful in improving post-stroke intervention.

6. POST-ICH STROKE TREATMENT

The existing post-ICHS intervention and treatment may be informed by the above analysis suggesting some measures undertaken quickly following the inception of the ICHS symptoms. A cocktail of medications ("*ICHS kit*") may be developed and provided to the individuals with indication for ICHS. In general, the following three active intervention steps are suggested:

Step 1: Reduce arterial pressure to absolute minimum with the objective to quickly reduce bleeding and thus, intracranial pressure helping to reopen the collapsed blood vessels on the venous side.
Step 2: Rapidly lower body and head temperature helping the brain to survive at the conditions of severely reduced brain circulation.
Step 3: Attempt to stiffen the walls of the blood vessels to prevent their further collapse helping to maintain at least some blood circulation in the brain.

The suggested three-step treatment is intended to maintain some blood circulation in the brain and provide a time window critical for stabilizing the patient's condition. Surgical intervention and administering of long-term treatment can follow the acute emergency phase as needed.

Another complementary immediate post-stroke treatment may be an induced dilation of the collapsed cerebral venous system possibly enhancing blood circulation.

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ADDENDUM

Intracranial Micro-Hemorrhagic and Micro-Ischemic Strokes

Small, short non-life-threatening **hemorrhagic strokes** produce longer-lasting and more debilitating global effects than similar **ischemic strokes**. In this addendum we focus on small magnitude strokes, both hemorrhagic and ischemic.

We suggest that in general, Intracranial Micro-Hemorrhagic strokes are leaving longer-lasting, spatially more global debilitating effects in the brain than Micro-Ischemic Strokes. This observation also applies to large, catastrophic hemorrhagic and ischemic strokes in that the size of the brain area affected by each type of stroke may differ significantly, as would their debilitating effects.

As observations indicate (need research & references), a clot developing in an arteriole or a capillary mostly deprives the area of the brain immediately adjacent to the clotted blood vessel, downstream of the clot location and upstream of it extending to the arteriole or capillary's branch-off location. Note that the area upstream of the clot may be affected less since there may be some limited blood circulation remaining in that part of the vessel.

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