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Human Anatomy Open Access Journal

# Radio-Surgery Vascular Targeting Biology

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**Editorial**

Volume 1 Issue 1

**Received Date:** December 02, 2016

**Published Date:** January 20, 2017

## Editorial

Arteriovenous malformations (AVMs) occur when arteries in the brain connect directly to nearby veins without the normal capillaries between them. They usually develop before birth; however, symptoms may occur at any age with catastrophic hemorrhages affects in children and young adults. Syringomyelia is damage to the spinal cord caused by a fluid-filled cyst that forms in the cord due to congenital abnormalities, spinal cord trauma or tumors.

While the conditions are comparatively rare, both had catastrophic effects. "AVMs affect between one in 1000 to one in 10,000, which is as common as Multiple Sclerosis (MS). Like MS, rapture of AVM mostly affects young people suddenly and catastrophically – causing either instant death or severe disablement. However, little attention has been given to research on AVM compared to MS. Similarly, syringomyelia can exacerbate immobility functions in the spinal injury patients.

The focus of AVM research has been to prevent rupture by either removing the AVM or interrupting blood flow. However, these processes were surgically inaccessible whereas other treatments such as injecting glue into blood vessels or using radiation to block them were considered less effective. The research team at Macquarie University Hospital has been engaged for some time to design a new in vivo molecular imaging technique which could identify AVM proteins that could be manipulated to encourage clotting to seal off the vulnerable blood vessels. The main goal of the project is to develop a new treatment for high grade brain AVMs that are untreatable using current methods. As a first step, stereotactic radiosurgery is used to stimulate molecular changes on the surface of endothelial cells in the AVM vessels. The second step in the process would be to target those molecules with antibodies attached to molecules that stimulate intravascular thrombosis such as tissue factor. If proteins in an AVM are unique they can be targeted directly, but the cells are fairly normal so radiations are to stimulate protein expression that makes the AVM cells different than normal cells. Identifying exactly which proteins change after radiation and by how much they change is quite difficult. However, last year the group worked to develop an *in vivo* molecular imaging technique which allowed studying different aspects of radiation-induced endothelial molecular changes.

During the last year, the team has used endothelial tissue cultures treated with radiation to show that we can image live cells with fluorescent-labeled antibodies to certain molecules and then applied the technique to the rodent model of AVM. This technology is used for the first time to provide quantitative information about molecular changes. The team had now identified highly prospective molecules for pro-thrombotic therapy. It is also believed that the technology and methods used could have a significant impact on other areas of medical research. This includes treatment of particular brain tumors. For example, at times it is very difficult to design effective delivery systems for chemotherapy to the brain. However, by blocking the blood supply to tumors, this problem can be resolved.

Prof. Stoodley and his team of research scientists and students is now using this technique to advance their understanding of syringomyelia especially its causes and movement of fluids within spinal cord. The use of in vivo molecular imaging technique can be used to image the entire spine with molecular tracers showing both the movement and quantity of fluid. Syringomyelia is one of the most enigmatic neurological conditions because the origin of the fluid that forms the cyst and the mechanism behind cyst formation have remained obscure. It has been

assumed that the fluid is cerebrospinal fluid (CSF), but that has not been proven. Building on the techniques developed in the AVM project, the group has also developed techniques for studying CSF movement which will allow quantitative assessment of fluid flow in the subarachnoid space and the spinal cord. The technique will also enable quantification of fluid flow out of the spinal cord, allowing for the first time to study the balance between CSF flow into and out of the cord. Our goal is to understand how syringomyelia forms so that we could perhaps prevent it, but this research could also be useful in other areas of medical research such as in the treatment of hydrocephalus, Alzheimer's disease or any conditions that require the delivery of drug therapy into the central nervous system.

## Acknowledgement

*Working with Prof Stoodley and his research team has been an exciting experience for me both professionally and socially. I am indebted to Prof. Marcus Stoodley, Head of Neurosurgery unit at Macquarie University Hospital Sydney, for nominating me for this prestigious fellowship. I was lucky to join this team after Prof. Stoodley's group was given the premier "John Mitchell Crouch Fellowship", in recognition of their ground-breaking research to develop new treatments for brain Arteriovenous Malformations (AVMs) and advance understanding of the pathophysiology of syringomyelia. Since 1979, every year this Fellowship is given to a renowned surgeon who is making an outstanding contribution to surgical advancements and research. I am also grateful to the Australian Government for awarding me the most prestigious Endeavour Executive fellowship, which helped me to advance my skills and experience in radiosurgery vascular targeting biology.*