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Birth and Growth of Neuroimaging and Vascular Intervention at Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram—Part I

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Abstract

This article is a historical narrative that traces the growth of neuroradiology and interventional radiology at the Sree Chitra Tirunal Institute of Medical Sciences and Technology, Thiruvananthapuram. From its humble origins in the pre-CT scan era of the mid and late 1970s, when invasive diagnostic procedures such as percutaneous carotid angiography, myelography, pneumoencephalography (PEG) and ventriculography were the mainstay of neuroimaging, the authors take the reader through their gradual foray into catheter four-vessel angiography and later free-flow embolization of arteriovenous malformations (AVMs), and finally to the use of microcatheters for selective embolization procedures. The equipment used in those early years—fluoroscopic tilting table, roll-film cameras, serial changers, PEG tables—provide an insight to an era with all its challenges before the advent of digital imaging. The authors' efforts to indigenize some of the hardware such as metallic stents and embolization material such as hydrogel spheres and lyophilized dura are also highlighted. The development of peripheral vascular intervention alongside neuroradiology is also highlighted. The authors pay tribute to an early pioneer of neuroradiology in India, Prof. Mahadevan Pillai, who was a guiding light to them during those nascent years.

Keywords
- neuroimaging
- vascular intervention
- interventional neuroradiology

> Our memories give us voice and bear witness to history, so that others might learn. So, they might celebrate our triumphs and be warned of our failures…………. "Heroes."

Early Years

Prof. Mahadevan Pillai laid the foundations of neuroradiology in the Department of Radiology at Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram in the year 1975. Born in Kayamkulam (Kerala) in 1908, Prof. Pillai had his medical training in the year 1934 at Andhra Medical College, Visakhapatnam. After obtaining Diploma in Radiology from the United Kingdom, he worked in the Department of Radiology at Barnard Institute of Radiology, Chennai. It is here that he introduced and popularized the techniques and applications of neuroradiological investigations. Association with giants among European neuroradiologists such as J.W.D. Bull, Pendergrass, Lindgren

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and Seldinger helped Prof. Pillai pioneer and establish several neuroradiological techniques in our country. Later, he became professor of radiology at National Institute of Mental Health and Neurosciences (NIMHANS) and subsequently Medical College, Thiruvananthapuram.[1-7] On the request of the Director, he joined Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, as the Head of Department of Radiology (►**Fig. 1**). The senior author of this narrative (V.R.K.) had the privilege to join him soon after in 1977 and work under his able guidance.

Percutaneous Carotid Angiography and Manual Film Changer

Apart from being an astute radiologist Prof. Pillai was also a great innovator. With the help of a local technician, he designed a manual changer that could hold with springs and cassettes in series for serial angiography. The changer box had a stationary grid compartment and held 5 cassettes stacked over one another, each having a handle of its own. A wooden headrest with a provision for comfortable neck positioning in the lateral view was also innovated by him. As a young radiologist, while V.R.K. would inject ionic-contrast medium into the carotid artery through a needle percutaneously and give command to expose/shoot, an assistant would pull the cassettes one after another rapidly after each exposure over a period of 6 seconds to obtain arterial, delayed arterial, capillary and venous phases of a cerebral angiogram (►**Fig. 2**). It took nearly 20 minutes to process each film series in the dark room and plan the next step after looking at the wet films. Prof. Pillai equipped the department with a 90°-90°tilting table (Diagnost 73, Philips) for myelography and general purpose radiography. The radiographic/fluoroscopic equipment had a railing system supporting an over couch X-ray tube for overhead radiography which could be used for cross-table horizontal beam radiography for lateral projections as well. This equipment was put to good use for cerebral angiography. After obtaining the frontal view of cerebral angiography, there was no alternative but to turn the patient's head and neck to contact lateral position with the table. The 3-piece 18G percutaneous angiography needle (Cournand needle) was well stabilized, but precariously, while the neck was acutely turned into lateral position with the needle in the carotid artery. Dr. George Mathews, Professor of Neurosurgery, would desire to know the lateral extent of intrasellar pituitary tumors, due to his special interest in transsphenoidal surgery for these tumours. Realizing that such tumour extension is best seen in axial views (submentovertical projection), both common carotid arteries would be punctured simultaneously, needle positions secured safely, and the patient's head carefully hyperextended into a hanging head position onto a smaller table at the head end of the main table, and arterial phase images obtained by simultaneous injection into both common carotid arteries. A plain radiograph would always be obtained just before injecting contrast medium into the artery for manual subtraction, particularly useful in the full axial projection to eliminate superimposing bony shadows. The plain radiograph without contrast was exposed to controlled light in the dark room by a low intensity wall-mounted light bulb to obtain the positive image for subtraction. In the later years, a subtraction/copying illumination box system was procured which had a better control of light intensity with knobs indicating the exposure in seconds. A further technique of magnification was added while exposing the angiographic films, using the air gap technique on removing the stationary grid from the top of the serial film changer. Soon such angiography procedures with magnification and subtraction became routine. It may be noted that resolution of the image on magnification angiography depends on the size of the focal spot. In subsequent years, an advanced X-ray table/tube equipment (Mimer III, Elema Schonander) having 0.6- and 0.3-mm focal spots was the workhorse for angiography and tomography. Aneurysms,

Fig. 1 Prof. Mahadevan Pillai, Founder of Neuroradiology at Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram.

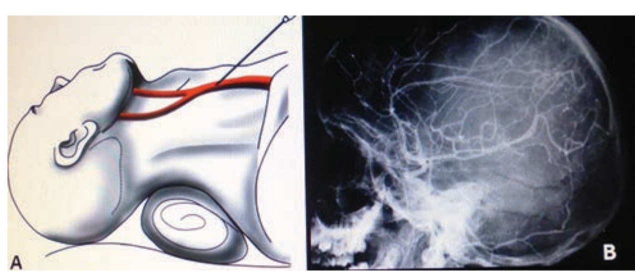

Fig. 2 (**A**) Schematic diagram shows the technique of arterial puncture for direct carotid angiography in the hyperextended position of neck (With permission from Dr. Harshit, SCTIMST). (**B**) Lateral view of carotid angiogram shows displaced Sylvian triangle, indicating a suprasylvian space occupying lesion.

arterial narrowing, and posterior fossa angiographic exploration were all performed by the above technique routinely, but at the cost of enormous time and radiation exposure.

70 MM Camera & Roll Film

A 70 mm roll film camera was interfaced with the distributor of the image intensifier of Diagnost 73 radiography table. The 70 mm roll film was exposed at 2 frames/second (maximum 6 frames/sec) after each injection. The exposed film would be automatically transported into a receiving magazine after exposure. The magazine would be disconnected and the roll film removed in the dark room to be mounted on a dedicated spool and bin for processing. It would be transferred into a circular tray-shaped spin dryer, following which the processed film could be loaded into a 70 mm film viewer (Heliophos) that was located in the conference room for discussion. However, the wet film could be quickly viewed during the angiographic procedure for planning further views. It was on this equipment that cerebral embolization of arteriovenous malformations (AVMs) were performed, quickly viewing the wet roll films to decide the endpoint of embolization.

AOT Automatic Serial Film Changer & Newton Hasty Stereotome

An unused AOT serial automatic film changer was coupled with the Mimer III tomographic/radiographic table with synchronization of its exposure (►**Fig. 3**). The AOT changer had loading and receiving magazines for the films. The film size was 24 × 30 cm, unlike the standard 14 × 14 inch size films that were routinely made in India.

These special size films had to be imported, manufactured by M/s Agfa/Sakura. It was possible to choose the rate of film transit per second at specified time intervals. Blank slots would be left intentionally in the loading magazine while loading the films to facilitate a proper venous phase at the end of 6 seconds and to conserve films. The stationary grid with a high 12:1 ratio could be removed for magnification angiography. The AOT film changer could be made vertical for horizontal shoot-through filming of the lateral view by mechanical cranking of the handle.

Newton hasty stereotome angiographic head cradle was noticed in the literature, and soon it was obtained for the department (►**Fig. 3**). Based on the principle of midline autotomography, the transparent head cradle could swing to right and left, and films in the AOT serial changer moved synchronously with each exposure, resulting in midline tomograms of each vascular phase. Hence, with one single injection, multiple angiographic tomograms were obtained. The patient's head could also be shifted off the midline into the tomographic plane if off midline structures such as M1 aneurysms needed to be visualized in the plane of section while the cradle was oscillating. Stereographic images in the arterial phase were obtained at 45°apart from each other, because of the cradle swing in the opposite directions if the CAM was changed into stereo mode. Later, these films were viewed on two adjacent view boxes. It was Prof. Mahadevan Pillai who taught me how to obtain stereoscopic vision by training the position of both eyes while focusing on the object of interest to bring out a third image as a 3D image between the two radiographs. The 3D vision of the angiographic films is no less than today's 3D rotational angiography in the modern single/biplane angiography equipment, visible only to the viewer but not to the others! It was a proud moment to have perceived the anatomical 3D course of the arteries, which enhanced the knowledge of neurovascular anatomy. This experience of magnification, tomography, and stereoscopic visualization of angiographic films was presented at the annual conferences of the Neurological Society of India and Indian Radiological and Imaging Association in the late 1970s.

Fig. 3 Patient is in position for stereoscopic and magnification cerebral angiography using a Newton hasty stereotome cradle mounted over a Mimer III table. AOT serial changer is seen for frontal projection.

Pneumoencephalography (PEG)

Mimer III was developed by Elema Schonander as a dedicated equipment for PEG examination. The 3-piece table could be folded into a somersaulting chair when the two hand held cranks were rotated. The backrest at the head end turned into

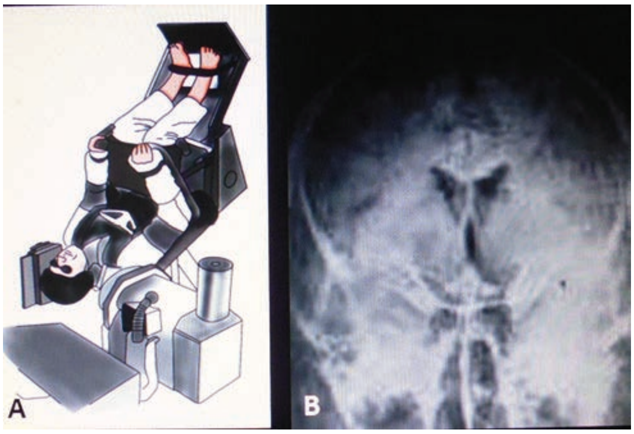

Fig. 4 Pneumoencephalography (PEG). (**A**) Mimer III somersaulting chair/table is positioned in Towne's position for visualization of the lateral ventricles as well as the aqueduct and fourth ventricle in frontal view. (**B**) Anteroposterior view of skull demonstrates air filled frontal horns. Third ventricle is appreciated in the midline. Cortical sulci are filled with air.

the back rest in the sitting posture, which had a rectangular central window for facilitating lumbar puncture. The side railings of the chair had sturdy buckles and straps to fasten and hold the patient in sitting posture as the chair rotated, driven by a motor, in both clockwise and anticlockwise directions (►**Fig. 4**). The somersaulting rotational maneuvers negotiated air from the lumbar subarachnoid space into the desired region of the ventricular system or cisternal spaces against gravity. Distortion or displacement of the air-filled cisterns or ventricles provided clues to the location of pathology. It was the practice to investigate hydrocephalus and small space-occupying lesions (SOLs) in posterior fossa using PEG. One would remember the scenes from the 1973 horror film The Exorcist.

Cerebral Ventriculography

Aqueduct stenosis, obstructive hydrocephalus, and posterior fossa tumors were investigated routinely by instilling radio opaque contrast medium into the lateral ventricle through a twist-drill hole and brain cannula (►**Fig. 5**). Experience of using iodinated water-soluble contrast medium (Conray 280) for ventriculography before the availability of nonionic contrast was presented at the Annual Conference of Neurological Society of India, which received great appreciation. Subsequently, a much safer nonionic dimer compound became available for this procedure.

Myelography

Oil-based contrast media (Pantopaque, Myodil) were the very early contrast used for myelography. Their manipulation into the cervical subarachnoid space required careful fluoroscopy and difficult radiographic technique for the lateral views. Iodinated ionic contrast medium was used in several of our patients, taking great care not to let it ascend into the lower thoracic region, since contact with spinal cord could cause seizures. Metrizamide (Amipaque, Nygaard) in powder form with solvent sodium bicarbonate became available in the 1980s and was prepared into a solution for immediate use (►**Fig. 6**). With this, it was possible to allow the contrast medium to outline the entire subarachnoid space, including the basal cisterns in the skull. In cases of lumbar canal stenosis, cisternal puncture was used to inject contrast medium in the cisterna magna in the sitting posture of the patient. Lateral C1–2 punctures were also performed in prone position of the patient for cervical myelography. This technique could completely fill the subarachnoid space all around the cord, unlike the oily contrast which settled by gravity in the dependent portion of the sacral region.

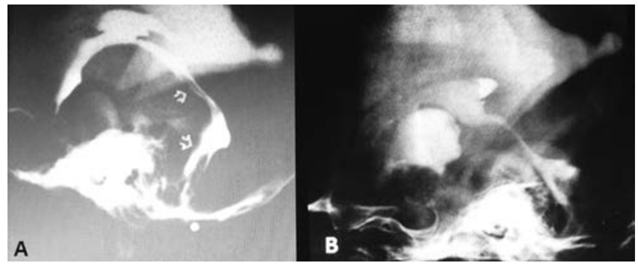

Fig. 5 Cerebral ventriculography. (**A**) Marked posterior displacement of aqueduct and fourth ventricle associated with hydrocephalus indicate space-occupying lesion SOL) in the brain stem in a child suggesting a glioma. (**B**) Suprasellar mass lesion indents into the floor of the third ventricle with a convex impression in a child suggestive of a craniopharyngioma. Normal anatomy of third ventricle, aqueduct, and fourth ventricle is appreciated.

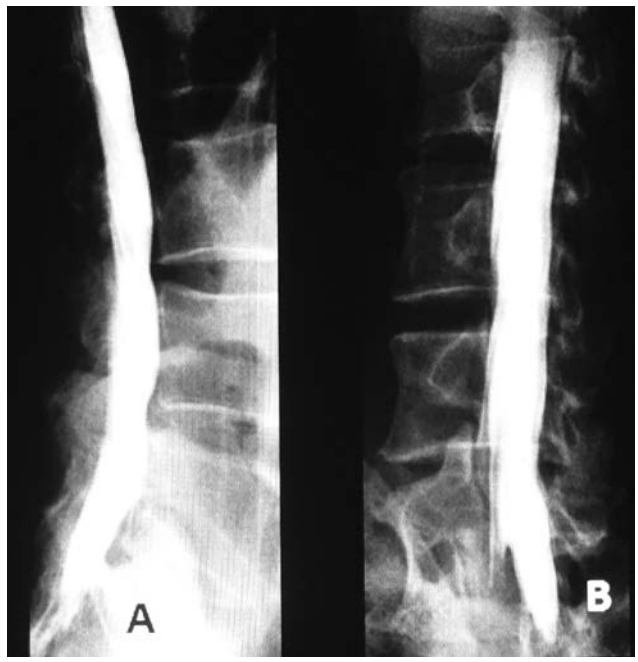

Fig. 6 (**A,B**) Lumbar myelogram. Water-soluble contrast medium demonstrates the thecal sac and nerve roots in lateral and oblique views.

Air Myelography

In patients of syringomyelia, dynamic variation of the width of the spinal cord was elegantly demonstrated, with the use of air as contrast medium for cervical myelography. Gardner's theory of hydrodissection of spinal cord was reemphasized on comparison of water-soluble contrast myelography and air myelography, wherein the cord collapsed in the latter imaging technique. Images were exquisite due to the additional tomography of cervical spine on Mimer III system. Associated Arnold–Chiari Type I was also demonstrated, while hydrocephalus could be appreciated in the same image, since a part of skull was included in the field of imaging (►**Fig. 7**). With the arrival of CT scanner, cross-sectional imaging of cervical spine of these patients showed even opacification of the syringomyelia cavity surrounded by the cervical subarachnoid space intervened by residual thin peripheral cord substance.[8,9]

Interventional Radiology

Few in his place could have been so farsighted and generous; more so, his enthusiastic support provided us all the opportunity to learn, experiment, and discover while he was the Director of the Institute as a Cardiac Surgeon. Dr. M.S. Valiathan, a National Research Professor and Hunterian Lecturer, was awarded the second highest civilian national award, Padma Vibhushan, for his rich contributions to health care, besides innumerable international recognitions (►**Fig. 8**). Birth of interventional radiology at our institute would not have been possible without his unstinted support to the Department of Radiology. Having assisted an abdominal aortography being performed by his senior teacher during his postgraduate course at Varanasi, the senior author (V.R.K.) took the first opportunity to make use of the available catheters and needles to start catheter angiography. Until then, only meager numbers of angiographic catheters were available, some as gifts from visiting consultants from abroad or a few ordered by our cardiology colleagues at our institute. Many were venous catheters for right heart catheterization to investigate congenital cardiac diseases by cardiologists.

Percutaneous Transfemoral Angiography & Balloon Angioplasty

There was no concept of arterial introducer sheaths, and routine catheters available were of 7 to 9 F size, made of woven Dacron or polyethylene. The puncture site was dilated with an arterial forceps in order to introduce the 7 or 8 F catheters through the skin hole directly into the artery over the guide wire. An exchange guide wire of 260 or 300 cm would be used to change catheters of different shape, as introducer sheaths were not available then, leaving fibrous tracks at the puncture sites often noted when repeat studies were performed on these patients.

A patient with severe short segment stenosis of the left subclavian artery in its second part presented with upper limb claudication.[10-12] When the angiographic image was shown to Dr. Valiathan in his office, with exuberant confidence that the lesion could be treated by balloon angioplasty, avoiding surgery, he did not hesitate to allow the authors to go ahead with the procedure, deferring his plan of surgery on the patient. Access was gained into the left axillary artery with the help of the Seldinger technique, and using textbook descriptions and literature knowledge, the focal stenosis was crossed by means of an extra-long guide wire. The rest of the procedure was smoothly completed (►**Fig. 9**). It can be noted that measurement of pressure gradient was a routine practice while treating occlusive peripheral vascular disease. Absence of pressure gradient following effective angioplasty was shown clearly on the recording and reappearance of radial

Fig. 8 (**A**) Prof. M.S. Valiathan, Director of Sree Chitra Tirunal Institute for Medical Sciences and Technology. (**B**) Surgical and Medical Blocks of Cardiac and Neurosciences.

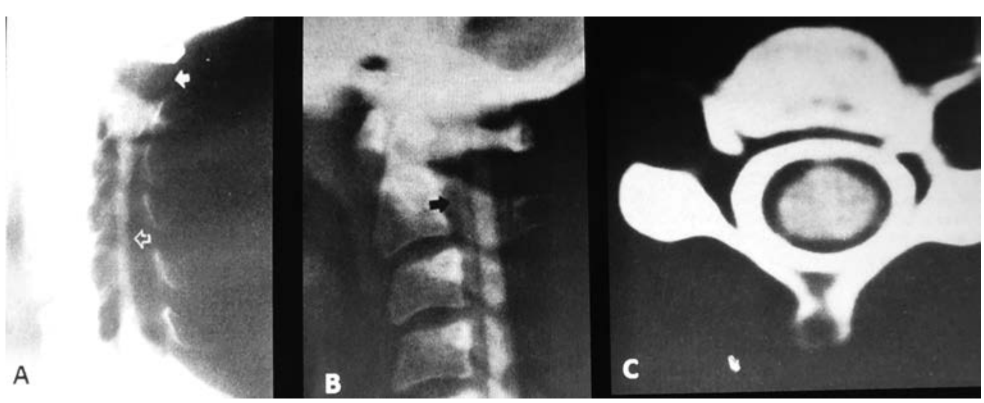

Fig. 7 Air myelogram. (**A**) Collapsed upper cervical spinal cord (open arrow) and Arnold–Chiari malformation I are shown outlined by negative contrast due to air in the subarachnoid space. Bulbous lower cervical spinal cord is revealed. (**B**) Metrizamide myelography demonstrates the contrast-filled syringomyelic cavity through the obex. The cavity is surrounded by thin cord and outer subarachnoid space. (**C**) Immediate CT scan confirms syringomyelia in the axial view.

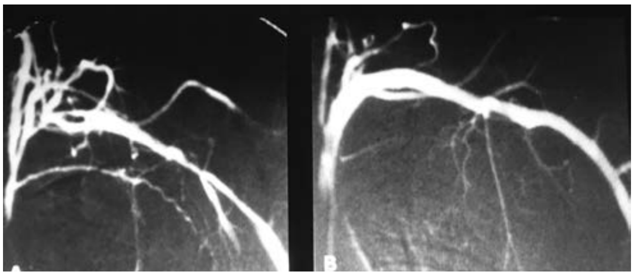

Fig. 9 Subclavian Angioplasty. (**A**) Short-segment narrowing of the second part of left subclavian artery is shown. (**B**) Restoration of lumen soon after percutaneous angioplasty is demonstrated.

pulse, with relief of symptoms being proof of the pudding more than the gradient recordings. It was the beginning of a service for a large number of patients presenting with lower limb claudication, ischemic ulcers, impending gangrene, etc., due to peripheral vascular disease and aortoiliac occlusions. Dr. Valiathan soon realized the potential of interventional radiology services that could be offered. He liberally sanctioned purchase of a wider range of catheters and all other necessary hardware to expand the scope of interventional radiology at the institute. It was his foundation that built the reputation of the institute for these novel treatment methods in the early 1980s itself. It was not difficult for him to be convinced to procure an advanced digital subtraction angiography (DSA) equipment–this too was acquired. Pathophysiology of peripheral arterial circulation was well understood by us and the necessity of a systematic hemodynamic assessment was felt. Dr. Valiathan provided us with an outpatient room for clinical examination, a treadmill machine to evaluate claudication distance and time, and a hand-held Doppler to assess ankle brachial index (ABI). This enabled the young radiology team to monitor pre- and postprocedural status of the patients. Apart from age-related peripheral vascular disease, many young patients with nonspecific aortoarteritis (Takayasu arteritis) were also diagnosed in significant numbers at our institute at Thiruvananthapuram. This condition, found mostly in younger patients with a female preponderance, could affect the aorta and any of its major branches. Balloon angioplasty was performed by R.M. (second author) in several of these patients, often repeatedly, with mixed results (►**Fig. 10**). Lessons were learned after aggressive angioplasty in a patient with bilateral carotid stenosis caused by nonspecific aortoarteritis, resulting in the rare complication of cerebral hyperperfusion syndrome.[13,14] This was highlighted in a case report published in cardiovascular and interventional radiology. Natural evolution of the same disease documented by angiography was also published by R.M. in Clinical Radiology after a mean follow-up period of 7 years. Similarly, popliteal entrapment syndrome in a few patients was treated by balloon angioplasty, demonstrating the typical focal deformation of the balloon. Having cardiologists alongside in the center, many of the young hypertensive patients were recognized to be having renal artery stenosis, and soon angioplasty of renal arteries was established as a line of treatment for renovascular hypertension and was

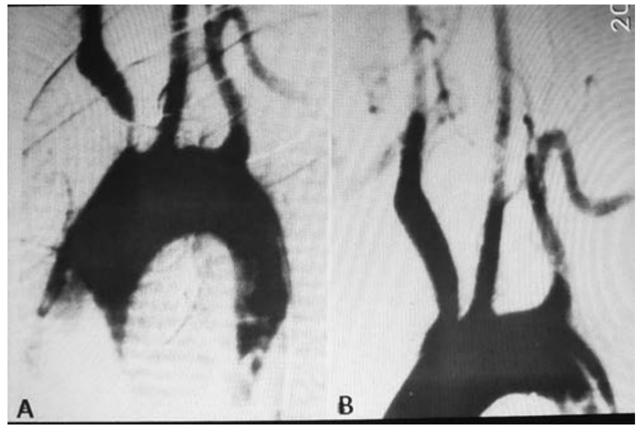

Fig. 10 Supra aortic Angioplasty. (**A**) Focal stenosis of innominate artery at its origin is noted. (**B**) An 8 F balloon angioplasty catheter was used to relieve the narrowing.

also supported by the nephrologists at the Medical College Hospital, Thiruvananthapuram. It is to be mentioned that the kissing double balloons technique for bifurcation stenosis and preservation of branch vessels, using a guide wire in situ during balloon angioplasty, were the novel ideas introduced by R.M. using information that became available in literature.[15-18] The cross-over technique to approach stenotic or occluded segments in the superficial femoral or iliac artery was also performed by him unwittingly, now named as a special technique. Puncture of the popliteal artery in prone position under fluoroscopic guidance for retrograde angioplasty of the femoral artery was also introduced at the same time. Today, ultrasonography is a convenient tool in this situation.

Laser Angioplasty

Prof. Valiathan, during an official visit to Moscow with a team of laser physicists from Bhabha Atomic Research Centre (BARC), witnessed the rapid progress made by Russian specialists in the use of laser in various medical disciplines. While its use in ophthalmology was already well-established, a promising application in the treatment of cardiovascular diseases, particularly revascularization of blood vessels was being explored at that time. He foresaw a great future in this technique, particularly if atherosclerotic plaque-specific laser systems could be developed which could ablate stenotic and occlusive lesions, obviating the need for bypass surgery. With this goal in view, a Neodymium YAG laser system was procured under a grant from the Department of Science and Technology, and a pilot project was started under the leadership of R.M.. Occlusive thrombotic material was obtained at surgery, and experimental animal occlusion models were used to gain experience in creating channels with the laser probe. An indigenous metal probe was also fashioned in the R&D wing of our institute (►**Fig. 11**). Delivery technique through a coaxial system with continuous saline flush for cooling the fiber tip was designed by R.M.. Finally, clinical trials were also conducted in three patients with successful recanalization. The procedure, however, went out of vogue due to the emergence of more effective alternate methods such as atherectomy devices and stents. However, introduction of laser technology brought other dividends—the successors at the institute and his team were using lasers for discectomy, tumour ablations, and a variety of other applications.

Thrombolytic Therapy of Peripheral Vascular Occlusions

Long-segment occlusions are due to thrombus in the lumen secondary to a severe focal stenosis or occlusion downstream. Despite restoration of the lumen at the short-segment occlusion, there remains the clot burden in the proximal artery. Catheter-directed thrombolysis was considered in these patients. Pulse spray technique was employed through the pigtail catheters having multiple side holes instead of using the expensive commercially available catheters. Thrombolysis of short and even long segment occlusions of peripheral arteries was performed using Urokinase which was then easily available. There were also instances of purely embolic occlusions, especially cardiogenic emboli that were thrombolyzed in emergency hours.

Fig. 11 Satelmond Palace gifted by His Excellency Marthanda Varma for research and development at the institute.

Spring Coils & Self-expandable Stents

R.M. played a stellar role in the management of peripheral vascular disease. While large aortic aneurysms were operated by the cardiovascular surgeons, smaller vessel aneurysms and arteriovenous fistulae (AVF) could be treated nonsurgically by emerging techniques such as coil embolization. He extruded spring coils from used guide wires by forcing them through core wires bent at an acute angle, having seen this technique described in interventional literature. These coils were used for occluding the feeding arteries of AVF and saccular abdominal, popliteal and carotid artery aneurysms (►**Fig. 12**). Follow-up of these treated aneurysms, however, revealed recurrence of the aneurysms. Gugliemi rightly discovered the most working and suitable detachable coils that are in use today. The idea of fabricating an in-house Gianturco-type self-expandable stent prompted R.M. to persuade me to obtain a welding machine for the purpose. V.R.K. recognized a mini-spot welder during one of his visits to the dental college for a dental checkup, and the department generously lent a spot welder for a weekend. The welding unit and the wires were hurried to home, and the stent models were fabricated overnight. It was necessary to test the stent in situ in an animal model before human trials. There was already a mobile fluoroscopy unit with digital subtraction equipment in the R&D wing of the institute. With the permission of the Director, as per regulations, the femoral artery of an anesthetized dog was punctured and the stent was introduced through a 9F catheter delivery using multiple guide wires as pushers (►**Fig. 13**). It was realized that the stent was in the inferior vena cava following deployment of the stent and control angiography. The animal under sedation was transported in a pickup van to a friend's radiology clinic for radiography, since it would not be possible to use an X-ray table meant for patients at the institute. With permission of the ethics committee, more such stents were deployed into the aorta and femoral arteries of dogs (►**Fig. 14**). At the Regional Research Laboratory (RRL), which was some 8 miles away from the institute, electron microscope examination of the dissected specimens of these arteries with stents after 12 months demonstrated neointimal proliferation and patency of the branching intercostal, renal arteries and iliac arteries, as described in the Western literature (►**Fig. 15**). Presentation of our experience at the Indian Radiology Association in the late 80s received

Fig. 12 Indigenous spring coils. (**A**) Extruded coils of different diameters and lengths from the core wire. (**B**) Lobulated aneurysm of left carotid artery at its bifurcation is noted. (**C**) Plain radiograph of neck shows the multiple coils delivered into the aneurysmal sac.

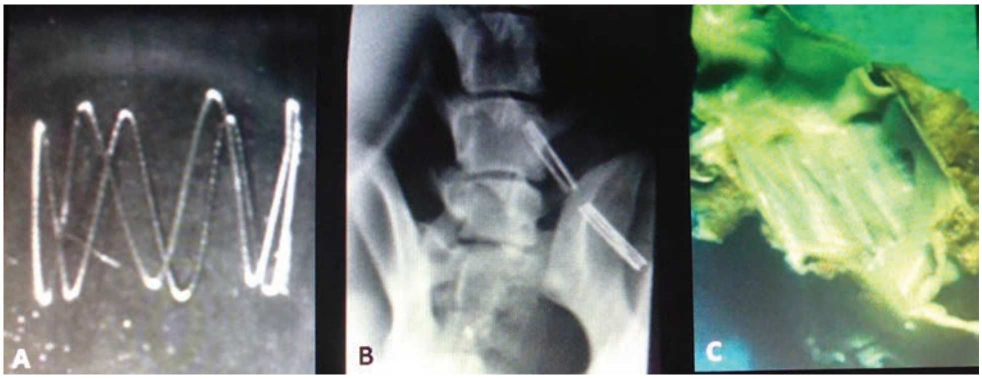

Fig. 13 Self-expandable stent implantation in a canine model. (**A**) Metallic stent welded out of a spring guide wire. (**B**) Two stents released into the left common iliac artery of a dog. (**C**) Autopsy specimen after 6 months demonstrates neointimalization and patent side branches.

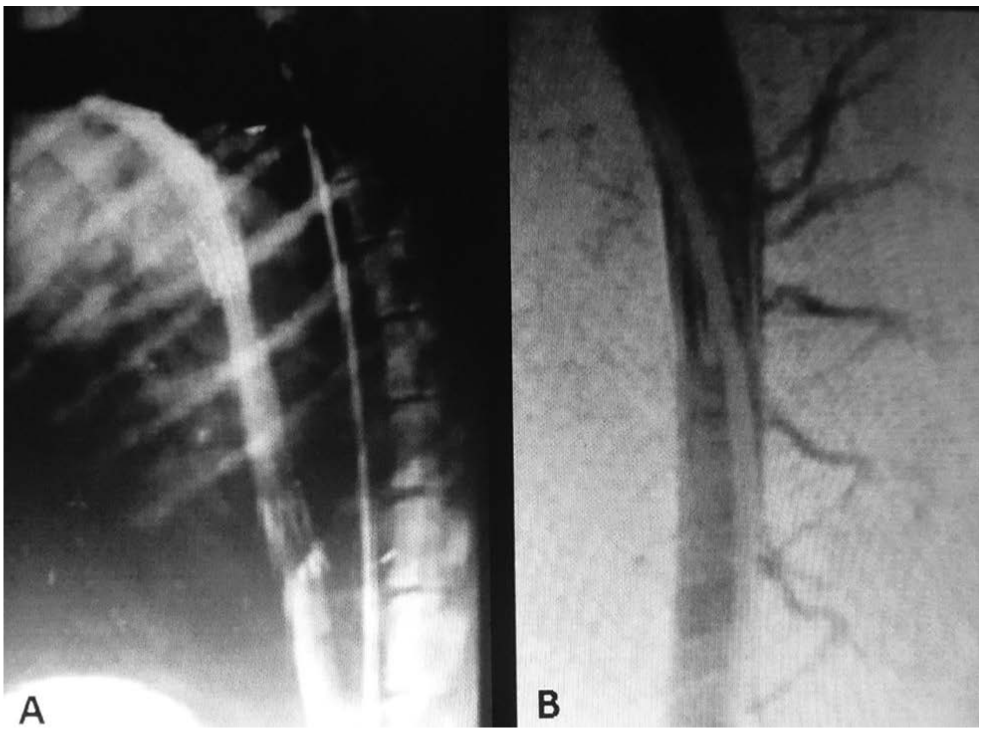

Fig. 14 Angiography in a dog. (**A**) Stents in the inferior cava. (**B**) Aortography shows patent intercostal arties 6 months following stenting the aorta.

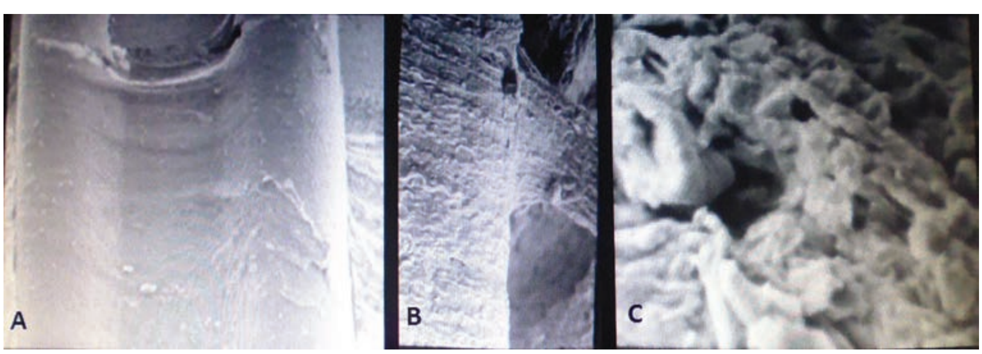

Fig. 15 (**A-C**) Electron microscopy of stented segment of aorta demonstrates veil-like covering of the stent limbs by neointima with rich cellular growth.

wide attention. Encouraged by the success of even such a crude device, V.R.K. consulted with the mechanical engineering group of Vikram Sarabhai Space Center to see if the home-made stent could be improved to the level of a balloon expandable stent of commercially available design, which was prohibitively expensive. Laser etching on a steel tubing was conceived, and a prototype was fabricated though further studies could not be carried out due to several other constraints. The quality and quantum of investigative and interventional radiological services are reflected by some of the publications listed in the bibliography given at the end of this article.

Conflict of Interest
None declared.

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