Story of Cyclotrons in India

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My first encounter with a hospital based cyclotron was in 1956 when I was a post graduate student at the British Post-Graduate Medical School at Hammersmith Hospital in London, where Clinical studies were being done with O-15. My friend Dr. SP Majumdar (who later on headed INMAS in New Delhi) also was at the Hammersmith hospital at the same time. Dr. Henry Wagner recently told me that his first stimulus was also to the Hammersmith Hospital Cyclotron two years after me, in 1958.

During my one year fellowship in Nuclear Medicine (1966-67) in Toronto and Montreal, Canada, I visited several centers in USA active in PET. Especially memorable was the St. Louis department of Michael Ter Pogossian who showed me PET metabolic images of the myocardium with labeled FDG and fatty acids.

My book "Principles and Practice of Nuclear Medicine" published in 1984 with foreword by Dr. Henry Wagner and appreciation by Dr. HN Sethna, Chairman Atomic Energy Commission (India) has one chapter on Cyclotrons in Medicine. The book contains NH3-ammonia PET images of myocardial perfusion and a picture of ischaemic viable myocardium with positive FDG-PET uptake and negative 1-123 fatty acid uptake. Dr. H N Sethna wrote – "It gives me great pleasure to write an appreciation for Dr. Lele's book on Nuclear Medicine, which is the first of its kind in this country. I have had the opportunity of seeing the work done in the Nuclear Medicine Department at the Jaslok Hospital & Research Centre when I presided over the 8th Annual anniversary function of that institution on 6th July 1981. I was happy to note the association of the Jaslok Hospital & Research Centre, right from its inception with the Bhabha Atomic Research Centre (BARC) Jaslok Hospital in 1973 was the first private hospital in this country to start a full-fledged, well equipped Nuclear Medicine & RIA Department and also the first hospital in the country to utilize the "radio-isotopic cow" for Tc-99m developed by the BARC, for intravenous administration of many new radiopharmaceuticals for various clinical investigations including the most modern and sophisticated nuclear cardiology. The expertise of the Nuclear Medicine Department at Jaslok was utilized for the evaluation of the RIA kits made by BRIT. It is most gratifying to note that Dr. Lele has been able to fully utilize the potentials of Nuclear Medicine for the benefit of Indian patients. I hope this book will inspire many more young doctors to emulate Dr. Lele's example. That would be the most appropriate way to implement the vision of Jawahar Lal Nehru and Homi Bhabha for the peaceful applications of Nuclear Energy. Dr. Lele is presently working on obtaining a Hospital-based Cyclotron and Positron Camera. Given his drive, initiative, planning and leadership qualities, and the backing given to him by the Chairman of the Jaslok trust, Seth Mathradas Assomull, and the

Trustees, I hope the dream becomes a reality within Dr. Lele's own working span".

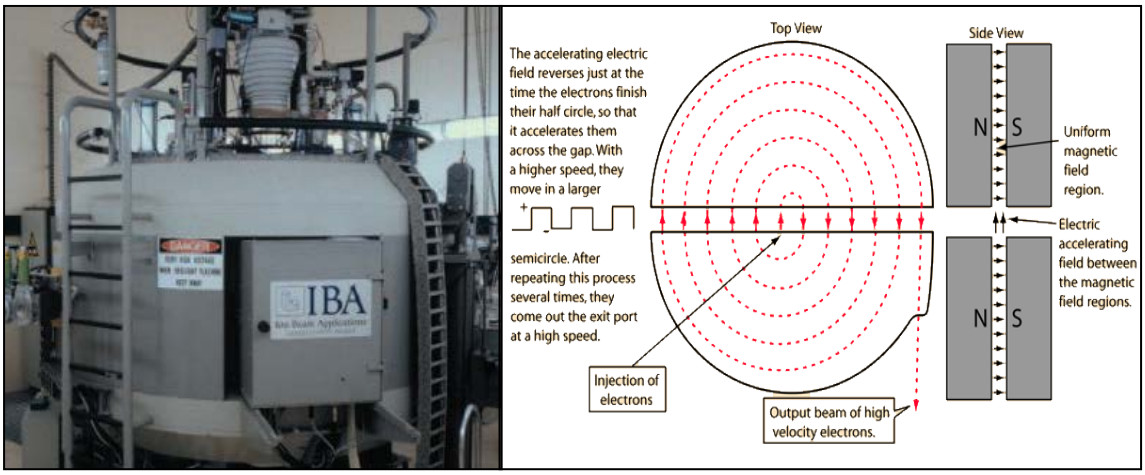
After Dr. Wagner's installation of an F16 Scanditronics cyclotron in the Nuclear medicine Department at Johns Hopkins Baltimore USA, in 1984, I also submitted a plan for the same cyclotron at Jaslok Hospital & Research Centre. The Swedish Government promised 25% of the cost of the cyclotron as an out right gift to promote the new technology in India. Since the Jaslok Hospital is located in a dense residential area, AERB was very reluctant to approve installation of this facility in the basement of the hospital so we started negotiation with the Films Division, Govt. of India located across the street for lease of land.

The Films Division was willing to be relocated to another site if we could make land available to them in Mumbai. Encouraged by this prospect, I sent my son Dr. Vikram who had already completed, his MD, DRM, DNB (Nuclear Medicine) for one year training in PET (1987-88). He spent six months with Dr. Henry Wagner at Johns Hopkins Baltimore USA and six months with Prof. Feinendegen at Julich in Germany. During his stay in Julich, Vikram completed a novel research project 'Effects of Rajayoga Meditation on cerebral glucose metabolism – study with FDG-PET'. This was later on published (Herzog H, Lele VR Kuvert T et al Neuropsychobiology 1990, 23, 182-187).

By end 1988 I had a meeting with Prime Minister Rajiv Gandhi at his residence in New Delhi, arranged by my friend Sri Vasant Sathe who was in his Cabinet. Rajivji said he was greately interested in the study of the mind. I said PET provides the most suitable means for the study of the mind and mental processes. I showed him the colour PET images of the brain showing the striking effects of meditation, an ancient Indian practice. I said my son had to take six Bramha Kumaris from Frankfurt to Julich for this study which could have been done in Mumbai on a much larger scale for which I need the Films Division land. He was greately enthused and committed his full support to my Jaslok PET project. But Fate ordained differently. With his sudden passing away my Jaslok PET project also perished.

On 10th July 1994, Dr. Vikas Sinha, Director of Variable Energy Cyclotron Centre in Calcutta inaugurated the National Symposium on Radionuclide therapy organized by the Eastern Chapter of SNM India. At that time Dr. Sinha attended my talk "Past, Present and Future of therapy in Nuclear Medicine". He was kind enough to ask for my perceptions about the future needs of cyclotron-produced radionuclides in the Indian Context, since VECC planned to acquire a new 32 MeV Cyclotron facility which would produce, in addition to C-11, N-13, O-15 and F18, three long-lived radionuclides Tl-201 (T½ 72 hrs.), Gallium-67 (T ½ 75 hours) and I-123 (T ½ 13 hours). I gave him the full briefing especially emphasing the need for I-123 (see my Editorial : Cyclotron-produced radionuclides in India : which way to go ? IJNM July 1994, 9, 144-145, and a list of I-123 labeled SPECT neuroreceoptor ligands on page 202 in same issue). I had read reports of Thallium-201 and Gallium-67 produced by VECC, used successfully on patients in Calcutta.

Enthused by this development and anticipating the availability of I-123 labelled ligands for imaging neuroreceptors in the brain, I installed a triple-head gamma camera at Jaslok Hospital & Research Centre in 1996 (first of its kind in Asia outside of Japan). But the I-123 supply from VECC was nowhere within sight. After eight long years of frustrating wait, on 1st January 2002 I met Dr. Anil Kakodkar, Chairman AEC along with a top IBA representative who offered to install a 32 MeV Cyclotron in Mumbai at their own cost, which would be run under total control and supervision of the Atomic Energy Department and which would produce long-lived radionuclides apart from fluorine-18 FDG. Dr. Kakodkar said that since the DAE is already committed to start a 32 Mev Cyclotron at Calcutta it would be difficult for him to support another cyclotron in Mumbai (even if it was offered free of cost). I pleaded with him not to rely on VECC Calcutta since, with due respects to Dr. Vikas Sinha, the non-performance of VECC over the years gave it zero credibility in the eyes of the Indian nuclear medicine community. According to the 2006-2007 AERB Report, authorization for construction of 30 Mev medical cyclotron facility at VECC was given on March 7, 2007. I feel greately disappointed that the IBA offer of 2002 was ignored and we unnecessarily lost five valuable years. At the 2006 SNM meeting at Jamshedpur Dr. Kakodkar was gracious enough to publicly accept the veracity of my criticism about the way the medical Cyclotron has been handled by DAE.



The Iya Committee Recommendations:

In 1998 the DAE appointed a committee under the Chairmanship of Dr. VK Iya, to advise on two projects proposed by BRIT in the 9th Five Year Plan.

1. A 32 MeV Cyclotron at NIMS Hyderabad which was later on given up.
2. RMC BARC TMH – Campus Mumbai.

Considering the need for both short-lived PET radionuclides (C-11, N-13, O-15, F18) and SPECT radionuclides (I-123, In111, Ga67) The RMC / TMH project – coordinator Mr. BN Karkera had shown preference for a 19 MeV Cyclotron. The committee proposed a 10-19 MeV Cyclotron which would fulfill both the needs.

One supplier (EBCO- Vancouver, Canada had given a written undertaking that his 10-19 MeV machine would produce 170 mCi I-123 at EOB after 3 hours irradiation and 200 mCi In111 at 48 hours from EOB after 8 hours irradiation. They would give a warranty period of 5 years and guarantee to supply the targetry and approapriate target transfer facility for the SPECT radionuclides.
The guarantee would also include demonstration of operational performance and actual production of SPECT radionuclides (esp I-123) in claimed quantities and radionuclide purity in a few trials runs.
The Iya committee recommended that tenders may be called for a 10-19 MeV machine with the supplier giving all the guarantees and 5 year warranty as stipulated above. If the RMC is interested only in short lived PET radionuclides then a 10 MeV Cyclotron is adequate. The ultimate choice of a 16 MeV Cyclotron was not according to the Iya Committee recommendations.
Today all 5 Cyclotrons in India are 16 MeV and their main preoccupation is with fluorine 18 FDG. It is not clear whether a 10-19 MeV Cyclotron is not available or whether the marketing skills of powerful multinationals have over-shadowed scientific wisdom.

Beyond FDG : FLT and PET:

At the time of the installation of the PET facility in RMC / TMC, I had publicly emplasised the need to ensure the availability of fluorothymidine (FLT) or fluoroethyl tyrosine (FET) along with FDG right from day 1 in order to overcome the problem of distinguishing FDG uptake in cancer from that in inferction / inflammation, especially tuberculosis. Tumor cells as well as leucocytes and macrophages avidly take up glucose (FDG positive images) but only tumor cells take up excessive aminoacids (like tyrosine) and nucleic acids (thymidine) hence (FET/FLT positive) while leucocytes and macrophages will not take up FET/FLT. Hence I had suggested back to back studies to test the hypothesis :
FDG + FET + = malignancy.
FDG + FET - = infection / inflammation
My preference is for FET which allows rapid visualization of tumours within 10 minutes of injection. Mucin-secreting tumours do not take up much FGD but-take up FET hence are the preferred tracer for detection of malignancy.
During the European Symposium on Radiopharmaceuticals at Lucca (Italy in April 2005). I saw on display a desk top Russian module which converts F-18 into FET. I asked them to immediately contact BRIT as a potential customer. I suggest all 5 Cyclotron facilities in India use this module to produce FET and do back to back studies in every suspected patient of cancer. If data is pooled from all PET centers with the next 8 months, India can give a new message to the rest of the world wether FET, not FDG is the preferred modality for cancer detection & staging.