August,2012

News Letter

Vol. XVI No. 6 Price: 50 Paisa

Rajiv Gandhi Cancer Institute and Research Centre

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Registered under "Societies Registration Act 1860"

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EDITORIAL

DIAGNOSIS, PROGNOSIS AND PROTOCOLS – The Triple Assault

Oncologists devastate their patients by launching triple assault of diagnosis, prognosis and protocol. Young doctors interpret the results of tests and convey the diagnosis as "stage IV lung cancer with poor prognosis". Many of the oncologists even give chemotherapy protocols and hand over leaflets of product information. That is great reading to be handed over to a patient when he has just been told that he has cancer. Patient tries reading a chemotherapy protocol. Protocol talks of the product pharmacology, how it is administered and its side effects. There is not a single word in it suggesting that it will help – it gives only destructive information. No wonder patient might feel he would rather die a quick death than submit to the tortures described in these documents. There are brave souls who submit themselves to suffer from virtually every one of the possible side effects.

Unfortunately, when doctors look at their patients, they see only the disease in them. Many of them need to be reminded that there is a human being in the room with them. Patient is not just a disease like NHL or sarcoma or squamous cell carcinoma of lung but a person. A medical college teaches everything, we need to know about writing prescription but nothing about understanding people.

Doctors take down the facts of patient's medical history without paying much attention to the patient. But we must never forget that the look of the patient's face, the tremble in his hand, the falter in his speech, the dropping eyelids and the hidden signs of what troubles him. Much of the communication between doctor and patient is non verbal. Many times we see patients from other states and countries with language barrier. We may show our concern through non verbal forms of communication.

It is well accepted that the practice of medicine has changed dramatically by advances in the doctor's ability both to diagnose and treat disease. Unquestionably the curative powers of the physician are vastly greater than ever before. But our power to heal people and their lives seem to have diminished. The patient is repaired but not healed and he is not a better person than he was before.

Every doctor thinks cure as healing power. Every patient they lose represents a profound failure and curing becomes an addiction. Since all doctors are bound to lose some of their patients, they develop a sense of failure as tally of loses rises. Is medicine not a failure oriented profession where we measure our success not only with cure rates, but also with morbidity and mortality? Because we emphasize on disease rather than people.

Let us cure the disease and care for the person. Let us understand the human angle of the disease. Disease is more than just a clinical entity. It is an experience and a metaphor with a message that should be listened to. We should be willing to treat more than their disease, by supporting them (emotionally) and loving them in addition to caring for their physical problem. We may be able to redirect their lives, not just treat illness.

Few years back I received thanks letter from one of relations of a patient, "I am indebted to you for providing my Mataji with the most effective medicine – sincere care, positive attitude and concern – God bless you and thank you for your kindness, concern and above all for being my mother's friend".

Dr. Dewan A K

BEYOND ^{18}F-FDG: FOCUS OF MOLECULAR IMAGING IN THE NEXT DECADE

During the last decade, several PET radiopharmaceuticals entered the phase of clinical trial, promising to become an integral part of management of cancer patients. FDG PET found its way in different applications related to cancer management in India and is currently widely practiced.

Although time has come to look beyond metabolism and target other functions of a cancer cell like proliferation, hypoxia etc, not much has happened in the country in the last few years. It is highly essential that in the next decade we target newer ligands for PET imaging to bring them from the bench to the bed side. With the help of these tracers, knowledge is being acquired on the molecular characterization of specific tumors, their biological signature and post intervention response. The potential role of these imaging probes for tumor detection and monitoring is progressively being recognized by clinical oncologists, biologists and pharmacologists. The scope of information to be covered will certainly need to include the assessment of therapeutic response in a particular tumor type or a specific process in the biology of tumor. The focus will also be on different new treatment modalities/ targeted therapies and precise delivery of external beam radiotherapy targeted towards a particular process in tumor biology.

If we look into various aspects of tumor biology it is amazing to note that a tumor cell follows a particular pathway to grow and another process to die, whether undergoing a natural death or a death post intervention. The study of glucose metabolism is very well established by now as well as mapping of few receptor type with the help of molecular imaging and is used in routine clinical practice. Other processes are in the process of validation with encouraging results. Let us take a look into few of the ones which have the potential to be clinically relevant in day to day practice. At the same time these ligands, to be clinically useful, needs to be either prepared commercially or in a hospital radiopharmacy with a reproducible radiochemical purity and sterility.

Amino acid and protein metabolism measured by 3-deoxy-3 (^{18}F) fluoro thymidine ^{18}F FLT measures tissue and tumor proliferation relying on enhanced proliferating activity which is more specific to a malignant tumor. This amino acid is rapidly incorporated into the newly synthesized DNA and 11-C thymidine could be produced. However, this being unsuitable due to short half life and rapid in vivo degradation, the more stable 18F labeled thymidine should be routinely used. The uptake of this tracer correlates with proliferation when compared with ki-67 index measurements in biopsy specimens 1-(2-deoxy-2 fluoro-B-D-a rabinofuranosyl) thymidine (FMAU) can also be labeled with ^{18}F and can be used to measure proliferative activity. (^{18}F) fluoro methyl and (^{18}F) fluoro ethyl tyrosine can also show amino acid metabolism of tumors.

As stated previously, the technique of precise delivery of radiation to the target is becoming more and more possible so that more of tumor tissue is irradiated and normal tissue is spared. In this setting the biology of the tumor is also important in predicting outcome of radiation. Tumor hypoxia is considered an important factor for resistance to radiotherapy and a risk factor for tumor progression.Thus imaging oxygenation of tumor is of great interest, especially for planning radiotherapy. Currently nitroimidazole derivatives like ^{18}F MISO & ^{18}F FAZA are the most common radiopharmaceuticals and the synthesis carried out via nucleophilic fluorination.

After ^{18}F fluorination protection groups are removed and the corresponding product is isolated via RP-HPLC, both tracers can be produced in high specific activity and radiochemical purity and the yield is much higher for ^{18}F MISO than ^{18}F FAZA. When oxygen is lacking in a tumor cell, however a second electron transfer reduces the nitroimidazole to a very reactive intermediate which binds to protein DNA with the cell and therefore becomes trapped intracellularly.

Thus 18F MISO uptake is inversely related to the intracellular partial pressure of oxygen. The same mechanism mediates the accumulation of FAZA by hypoxic cells. Currently, most studies are being carried out by MISO and may be in the next couple of years we can use this compound for dose painting in radiotherapy. Imaging of lipid metabolism of tumor can be labeled achieved by synthesis of choline with either ^{11}C or ^{18}F. It was used to visualize a variety of tumor including prostate cancer. To benefit from the longer half life of the tracer and to promote its routine uses, more importance have been given to ^{18}F.

Ability to image dopamine transporter system has been of benefit in evaluation of primary and metastatic NET's with usefulness also demonstrated in carcinoid tumors. It has highlighted more specificity in low grade gliomas thus helping in continued risk stratification in these patients. Similarly, somatostatic receptor imaging is establishing its role in routine clinical care. These radiopharmaceuticals pave the way for receptor based treatment labeled with a suitable radioisotope. ^{18}F-16 a fluoroestradiol ^{18}F FES has the potential to image oestrogen recptor status in breast carcinoma and has the potential to accurately predict response to modern breast cancer patients, especially those treated with aromatase inhibitors. Bench work

to map angiogenesis is going on but will be a while before it comes to the bed side. Similar is the fate of radiopharmaceuticals for imaging of apoptosis.

Talking about the use of these molecular imaging agents in routine clinical practice, we are faced with a paradoxical situation especially in this country. Very few hospital based institutions have a radiochemist on their rolls for in-house synthesis of these compounds. The infra-structure of GMP is expensive and commercially not viable. Therefore, the concept of hospital based radiopharmacy for formulation of these compounds for its regular use needs to be standardized. Today some companies have standard synthesis modules which are fully automated and can be used for routine synthesis in GMP compliant environment. With one set-up it is possible to easily label different radionuclides without having cross contamination issues by easily replacing the sterile single use cassettes. This makes these modules an ideal equipment for routine clinical production. The sterile single use cassettes are assembled under GMP compliant clean room conditions, sterilized with gamma radiation and double vacuum packed. The manufacturer guarantees a shelf life of twelve months. It should be possible to use these in a hospital radiopharmacy as reconditioning, cleaning and sanitation routines are not necessary due to the cassettes one time use. It is presumed that routine use of other F^{18} based tracers will be possible in times to come and we here are certainly going to take a step forward to make this a reality.

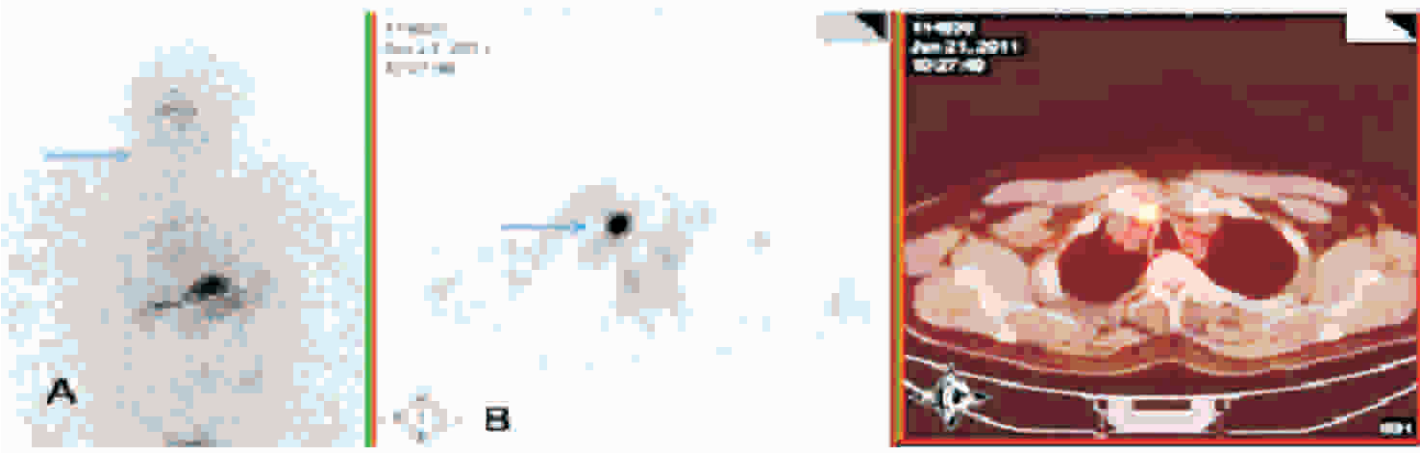

Figure: A case of radioiodine refractory thyroid cancer where I-131 scan is negative (A) & disease is seen in FDG PET (B & C)

PET imaging in the preclinical setting (micro-PET) is also increasingly being used in drug discovery to study tumor biology. As applications of micro-PET imaging in cancer models have increased, preclinical micro-PET equipment design and sensitivity have also improved, allowing higher resolution and throughput.

Micro-PET studies utilize the same radiotracers used in clinical PET, and provide the same versatility in imaging in vivo molecular and cellular function.

(Dr PS. Choudhury, Director of Nuclear Medicine)

CME for ICU Staff (14th July)

A CME was organized by Infection control team on 14th july in RGCI&RC for ICU Staff on waste management and safe disposal of sharps. We all know that 38% of sharp injuries occur during use, 42% occur after use before disposal. The most common cause of needle stick injury occurs during recapping of needles after use. The most important of these Pathogens are hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV. The estimated risk of infection following injuries with sharps is---

HIV--.3%
HCV----3%
HBsg---30%.

One of the major problems associated with the management of needle stick incidents, is the lack of hard evidence relating to the actual number of incidents & is due to under-reporting.

Dr. Neelam Sachdeva
Sr. const. microbiology

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Registered with Registrar of Newspaper Under No. 68797/98
Postal Department Registration No. DL(N)/004/2012-14
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SKIT IN WARDS (20TH JULY) ON HAND HYGIENE



A skit was organized in the ward on 20th july for pediatric patients ,their parents and other adult patients of the ward by infection control team. We all know HAND HYGIENE is the single most important intervention to prevent the spread of infection from one patient to another patient. To develop this quality improvement tool ,successful partnership is required between infection control team and rest of the hospital staff . To emphasize this, number of presentations and skits had been arranged in OPD areas and wards for patients and staff. Great appreciation and recognition goes out to RGCI& RC community for the hard work put forth for improving the hand hygiene .

Dr. Neelam Sachdeva
Sr. const. microbiology

FORCE (FORUM ON RENAL CANCER EXPERTS) 2012

Rajiv Gandhi Cancer Institute & Research Center organized a meeting on Renal Cell Carcinoma on 4TH August 2012 as FORCE i.e. **Forum on renal cancer experts**, which was held at hotel Taj Mahal Delhi. The ball was set rolling by overview by Dr D.C. Doval, Director, Medical Oncology which was followed by a scintillating talk by Prof. Manuela Schmidinger, Medical Oncologist from medical college, Vienna, Austria about the latest concepts in management of RCC. The Indian scenario was aptly covered by Dr Sudhir Rawal, Director, Surgical Oncology, with his exposition of cases treated at our institute. This was followed by panel discussion which was moderated by Dr Vineet Talwar, Sr Consultant, Medical Oncology to visit certain contentious issues pertaining to Renal Cell Cancer Management. It was a well coordinated, lively and interactive talk attended by doctors from all over northern India. The felicitation of the faculty was done by Dr A. K. Dewan, Medical Director, RGCI & RC.

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Printed & Published by Mr. K. K. Mehta on behalf of Indraprastha Cancer Society & Research Centre and Printed at Raju Art Printers, 18-A, Old Gobind Pura Extn., Street No. 2, Parwana Road, Delhi-51, Tel. : 9871006333, Published from RGCI&RC, Sector-V, Rohini, New Delhi-110085

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shoot, concept & design: patch creative unit 9811023882