

Scientific Session-9 Molecular Imaging in Therapy

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Road map to molecular imaging: historic and basic considerations

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The road map for the current development of molecular imaging goes back to the discovery of x-rays by Roentgen in 1895 which was followed by several developments in morphologic imaging that include US in the 1950's, CT in 1970's and MRI in 1980's. Radioactivity, the basis of physiologic imaging, was discovered in 1896 by Becquerel. Gamma camera was developed in 1950's and progressively led to SPECT capability and multi-head detectors. Positron emission tomography signaled the main birth of molecular imaging which was further strengthened by merging morphologic and functional modalities, use of newer radiotracers and addition of functional MRI and MR spectroscopy. Functional capability of US along with nanotechnology based and optical imaging have been added to the scope of molecular imaging technologies. Molecular imaging can then be defined as visualizing normal and abnormal cell functions in- vivo by utilizing biochemical and/or pharmacological probes. The instruments utilized for such imaging are mainly PET or PET/CT, SPECT, functional MRI, MRS, ultrasonography, optical and nanotechnology based imaging devices. Molecular imaging helps in individualizing patient management in cancer diagnosis and treatment that include planning radiation therapy to help define the entry ports and minimize the effects of radiation on normal surrounding tissue; diagnosis of cardiac diseases, neuropsychiatric disorders as well as in infection and drug development.

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PET/CT and Radiotherapy Planning

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Abstract not available

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The Importance of Quantitative Molecular Imaging: From MORE (Molecular Response) to PERCIST (PET Response Criteria in Solid Tumors)

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Abstract not available

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Use of PET/CT Imaging with ⁶⁸Ga DOTATATE in the evaluation of patients with neuroendocrine tumors

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Introduction: Radiolabeled peptides both for diagnosis and therapy of neuroendocrine tumors (NETs) has gained increasing interest. In the eighties, ¹¹¹In-Octrotide became one of the best examples of molecular imaging plus for Nuclear Medicine, representing the exceptional capability to detect over-expression of somatostatin receptors (SSR) in NETs. However, these compounds labeled with single photon gamma emitters have some restrictions due to intrinsic limitations of gammacamera, mainly as a consequence of its own physical characteristics, causing low sensitivity and poor resolution compared with PET images. On the other hand, the use of ¹⁸F-FDG PET imaging has poor detection capability due to the recognized low metabolic activity of these type of tumors. Consequently, a different agent, appropriate for peptide labeling with positron emitter for PET imaging, is highly desirable. In January 2008, we set up a ⁶⁸Ge/⁶⁸Ga generator designed to obtain enough quantities of ⁶⁸Ga to label the same polypeptides used to treat patients with NETs such as DOTATOC and DOTATATE. As far as we know, this is the first time that such a device is installed in Latin-America for specific PET/CT imaging.

Materials and Methods: Since then, we have studied 108 patients, 56 females and 52 males (52.2 ± 15.1 years) with proven NETs for staging, re-staging and treatment control of neuroendocrine tumors using PET/CT images with ⁶⁸Ga-DOTATATE. Primary tumor localization was carcinoid and NET in 90 patients, medullary thyroid carcinoma in 7, GIST in 1 and malignant thymoma in 1. Secondary lesions were mainly located in bone, liver, mediastinum, pelvis, peritoneum, lung, ovary, spleen, adrenal gland and others. Somatostatin (SS) analog peptides were labeled with the trivalent cation ⁶⁸Ga⁽⁺³⁾ and the bichelating agent DOTA using a semi-automatic module in an easy and safe way. The generator's eluate was purified and concentrated in a cation-exchange cartridge. The labeling process was done heating the complex in a dry oven; purification was carried out through a C₁₈ column. The radiochemical purity was higher than 99% ± 1.0%. Previous to the administration of the radiopharmaceutical, the patients were over-hydrated to improve the renal excretion of the tracer. An average dose of 3 mCi of ⁶⁸Ga-DOTATATE (Nuclear CGM, Santiago,

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Chile) was injected. PET/CT whole body images were acquired 45 to 60 minutes after the injection of the radiopharmaceutical in a Biograph 6 HiRez P3D (Siemens Medical Systems, USA) with 4 mm. LSO high resolution crystals and fast electronics (500 nseg). CT images were used for attenuation correction of the PET images. The SUV was calculated in the most representative lesion.

Results: In all cases PET/CT images were of excellent quality allowing the detection of very small tumors undetectable by alternative methods including primary tumors in patients with NET of unknown origin.

The images obtained with PET-CT technology in the detection of NETs have a better resolution, higher sensitivity and a better accuracy in the localization of the lesions.

Conclusion: PET/CT imaging with ^{68}Ga -DOTATATE in the evaluation of NETs is a very promising technique due to its excellent resolution and precise anatomical localization with the added value of fusion images. ^{68}Ga -DOTATATE is a cyclotron-independent radiopharmaceutical permanently available at a reasonable cost. The use of PET/CT ^{68}Ga -DOTATATE demonstrates that this technique shows better images than ^{111}In labeled peptides. This technique represents a big jump for NETs detection and follow-up. SUV measurements permit a reliable and quantitative method for a more objective evaluation of therapy response. Polypeptide labeling with ^{68}Ga is a simple and safe semiautomatic procedure. The semiautomatic procedure to label SS analog polypeptides with ^{68}Ga is a simple and safe producing very stable complex with high radionuclide and radiochemical purity. Additionally, the implementation of $^{68}\text{Ge}/^{68}\text{Ga}$ generators allow daily elutions of ^{68}Ga ready for "on-site" labeling of peptide and other potential molecules in the future.

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The limitations of CT to monitor radionuclide therapy in neuroendocrine tumours

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This title to most nuclear medicine physicians seems to be a "no-brainer" clearly CT is not good at monitoring anything! However we must be careful not just to use our prejudice to look at this question but try to look at the evidence. In addition can nuclear medicine offer a realist and reproducible alternative. Firstly what is the aim of using imaging to monitor the result of therapy. Initially this seems a facile question but in fact it is vital in understanding the issues involved. When a new anti-cancer drug is being developed it is important to know firstly does it work and secondly does it work better than what is being used routinely. The easiest measure would be to look at death rates, however this is a crude measurement and in reality in many cancers it would take too long to decide if one treatment resulted in less deaths than any other and indeed in NETs each trial would need to take 20 years. A quicker and simpler method would be to look at whether the cancers got bigger or smaller; if they get smaller good, if bigger bad. The next is to define what is smaller and what is bigger. The first criteria developed by the WHO was to look at a 50%

change in volume. However CT does not measure volume so a surrogate was a change in cross sectional area of a tumour of 33% (this related to a volume change of 50%). Disease progression would be a doubling of cancer size and response a reduction of 50%. The need to measure across tumour masses in two dimensions was complex and introduced error. Also 5 index lesions only were used. This meant that if these reduced by 50% but there was new tumour growth elsewhere it was still considered a tumour response. The South West Oncology Group in the USA redefined the criteria using a single axis change of 25% (in fact it should be 27%) and added other factors such as new disease sites this became RECIST.

RECIST which started off as a guide to help research has rapidly become a straight jacket used in disease management. For example if a patient has a cancer treated by chemotherapy and the tumour shrinks by 24% this is recorded as only disease stability and further therapy is denied. This use of RECIST was never meant by its originators and has resulted in its mis-use denying patients effective therapy.

In NETs the situation is worse as very few treatments result in a significant partial response on treatment. In the largest published review of the use of Lu-177 DOTATATE (Kwekkenboom JCO 2008) the recorded complete and partial response rate was 30% but almost all patients had an improved survival with an additional 40-72 months survival being recorded independent of CT response.

In our study (Navilkissor EJNM in press) There was a correlation between disease progression on CT and disease survival with patients dying 2 years early than those with disease stability or tumour response but no real difference between those having disease stability and partial response on CT. However improvement or not of patients symptoms after the first treatment was a much better predictor of survival than CT and it may be a cheaper and more valid alternative to CT in patients with NET may just be to ask "How do you feel".

Further interesting data has emerged from work done in Poland concerning patients treated with Y-90 octreotate where again there was little correlation with outcome and early CT changes. At 6 weeks after the final cycle of Y-90 octreotate most patients had disease stability on their CT (Cwikla et al An Oncol in press) but this did not predict outcomes. However over half the patients treated showed further spontaneous reduction in tumour size without any further treatment by the 6 month post last cycle CT.

There is a clear pattern emerging. CT on its own has a limited role in predicting the effect of radionuclide therapy. However early progression of disease seems to be a bad prognostic sign and should lead to reconsideration of persisting with that therapy. CT cannot predict final outcome at least initially but may be able to several months after the end of treatment. Other methods need to be considered including the use of symptom mapping, biochemical markers and also a reliable method of quantifying functional imaging which can be used with both single photon and PET.

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In the current world of PET/CT for therapeutic monitoring, who needs Tc-99m and the other non-positron emitting radiopharmaceuticals?

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Accumulative advances in available treatment options for cancer patients, in particular chemotherapy and radiotherapy, have led to improved outcome and survival. An important prerequisite in monitoring the effect of such treatment on tumor progression requires effective imaging methodologies. Currently positron emission tomography (PET) has proven to be a valuable functional imaging modality, but given the lack of PET and cyclotron for the production of PET radiopharmaceuticals in a large number of institutions, particularly in developing countries several other commonly used non-positron emitting radiopharmaceutical are available. The choice of which depends on the location and pathology of the cancer. In this report, we reviewed the use of these non-positron emitting radiopharmaceuticals (Tc-99m sestamibi, Tc-99m tetrofosmin, thallium-201, In-111 /Tc-99m octreotide, I-123/I-131 MIBG, Ga-67 citrate and Tc-99mV-DMSA) for successful monitoring of the response of various tumors to chemotherapy and/or radiotherapy. Therefore, these radiopharmaceuticals can provide useful alternative for therapeutic monitoring in those institutions that do not have PET/CT,

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Effect of external irradiation on radioimmunotargeting.

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External irradiation (XRT) has been advocated in combination with radioimmunotherapy (RIT) for many reasons. (1)(Ruan et al, 2000): Improved RIT: 1.Enhanced tumour uptake. 2.More uniform distribution of the radiobiomoiety in the tumour and of dose delivery. Improved results as compared to XRT alone: 1.RIT Boosting radiation dose to primary site by XRT 2.RIT irradiating tumour cells beyond the XRT radiation cone 3.RIT targeting metastases, known or hidden, beyond the XRT zone. This study was designed to look at tumour uptake rather than to overall therapy outcomes, but any benefit in combined therapies is of course predicated to efficient RIT uptake (and RIT dwell time) of the radiobioconjugate in the tumours. Aims: 1.To compare in vivo localization of radiolabelled antibodies in patients with or without XRT to the tumour field 2.To compare the in-vivo localization of such radiolabelled antibodies in experimental mice models (xenografts) with and without XRT (results described elsewhere). 3.To study the effect of XRT on circulating tumour marker levels (also described elsewhere) Methodology: Radioisotopes: Radio iodine I 131 for antibody labeling and Molybdenum 99/Technetium generator were obtained from BRIT,,Mumbai.India. Antibodies: A pancarcinoma Monoclonal Antibody M3(an

anticytokeratin 8-18 , IgG1) recognizing the TPS antigen was very kindly gifted by Prof Bjorklund,President Swedish Cancer Council,Sweden.,concurring with our advocacy of a pancarcinoma approach for simplifying the logistics of radioimmunotherapy.(Hazra et al ,1984,2) Radiolabelling : Radioiodination performed by the Iodogen method,[Paus et al,1982(3)} and Technetium labelling by the method of Schwarz and Steinstrasser,1987(4)(modified by Mather S.J,personal communication) 10 patients underwent radioimmunoscintigraphy first with Technetium M3 to confirm localization and then with Iodine 131 M3 for dosimetry. 5 of these underwent radioimmunotherapy with Iodine 131 M3.In this group prior to the second installment of radioimmunotherapy the tumour field received 3 Gy XRT 1 hour prior to s radiolabelled antibody. Results: Table 1 shows the temporal course of 131 Iodine labelled antibody accumulation in patients after a small dose of 1mCi corresponding to an antibody mass of about 0.3 mg. Even though the absolute counts decline with time, there is a steady increase in the fraction of antibody localizing in the tumour, from 8.6+- 3.01% at 1 hour to 50.6+-6.42% at 48 hours. Table 2 gives the percentile tumour ROI accumulation at various time intervals in 5 patients who received radioimmunotherapy for metastases. ROI analyses show a significant accumulation of the 131 I antibody over a period of 8 days, maximum values at 8 days being 52.4+-5.93% of total body counts It may be

Time Interval	Percent Tumour ROI/ Whole body counts
1 Hr	8.6 3.01
6 Hrs	15.1 4.65
24 Hrs	43.3 3.57
48 Hrs	50.6 6.42

Table 1. Radioimmunoscintigraphy with 131 Iodine M3:Percent Tumour Region of Interest (ROI) counts as a fraction of whole body counts at various time intervals in patients administered about 1 mCi M3 (n=10)

Time Interval	Percent Tumour ROI / Whole body counts
4 days	40.9 5.60
6 days	45.9 4.97
8ays	52.4 5.93

Table 2. Radioimmunotherapy with 131 I M3 : Percent Tumour ROI/whole body Counts in patients administered 50-150 mCi (15-50 mg) antibody (n=5)

Protocol used	%ROI at Time Interval s		
	Day 4	Day 6	Day 8
RIT 50 mCi	37.3	42.8	50.4
RIT 50 mCi 1 hour after 3 Gy XRT	46.3	58.5	62.4
Percent Increase	24.12	36.68	23.80

Table 3. Tumour localisation (percent tumour ROI/ whole body counts) in a representative patient with 2nd administration of 131-I M3 antibody RIT after XRT compared to 1st administration of RIT,before XRT.

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mentioned here that all these patients had received nonspecific human gamma globulin to block reticuloendothelial accumulation, [Hazra, 2004(5-7)]. Table 3 is a representative case of the changes observed when External irradiation was given prior to the second installment of RIT, and the uptake is compared to that after the first installment where RIT was given without prior XRT. Table 1. Radioimmunosciintigraphy with ¹³¹Iodine M3:Percent Tumour Region of Interest (ROI) counts as a fraction of whole body counts at various time intervals in patients administered about 1 mCi M3 (n=10) Time Interval Percent Tumour ROI/Whole body counts 1 Hr 8.6+3.01 6 Hrs 15.1+4.65 24 Hrs 43.3+3.57 48 Hrs 50.6+6.42 Table 2. Radioimmunotherapy with ¹³¹I M3 :Percent Tumour ROI/whole body Counts in patients administered 50-150 mCi (15-50 mg) antibody (n=5) Time Interval Percent Tumour ROI/Whole body counts 4 days 40.9+5.60 6 days 45.9+4.97 8ays 52.4+5.93 Table 3. Tumour localization (percent tumour ROI / whole body counts) in a representative patient with 2nd administration of ¹³¹I-M3 antibody RIT after XRT compared to 1st administration of RIT, before XRT. Protocol %ROI at Time Interval s used Day 4 Day 6 Day 8 RIT 50 mCi 37.3 42.8 50.4 RIT 50 mCi 1 hour 46.3 58.5 62.4 after 3 Gy XRT Percent Increase 24.12 36.68 23.80 Conclusions: With prior XRT there was a considerable increase in the percentage counts in the tumour ROI,maximal at 6 days. Discussion: Ruan et al, 2000(1) have discussed the opposing effects of increased capillary leakiness increasing radioimmunoconjugate localization, and presumed radiation induced debulking of the tumour increasing % ID/gram, versus the radiation induced rapid structural degradation of the tumour stroma and vasculature as well as decreased antigen expression diminishing antibody targeting. Clearly the optimal interval between XRT and RIT would depend on the relative tempo of these processes We have earlier described the merits of 4 different approaches explored by our group for enhancing tumour/nontumour ratios: XRT, pretargetting, economically blocking reticuloendothelial nonspecific uptake using nonspecific gamma globulin and using (Fab) 3 constructs. (Hazra, 2008,8). Clearly a combination of approaches could also be used in the future, as a logical sequel to smart bomb approaches to refine the biological moiety in radiobioconjugate targeting. (Hazra et al, 1995,9). Acknowledgement: Support of the ISORBE Wolfgang Becker Amersham award to PKH and of the ICMR to DKH is gratefully acknowledged.

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Rapid guide for drug interaction with radiopharmaceuticals

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Too many drug interactions related to radiopharmaceuticals take place every day in hospitals' routine, but many are not reported or even sensed. Information concerning these kinds of reactions is not abundant and nuclear medicine staff is usually overwhelmed by this information. To provide a rapid guide that could be used for all nuclear medicine we compiled the medical literature, using the criteria of a systematic review established by the Cochrane Collaboration on pharmaceutical-drug interactions to provide a summary of documented interactions by organ system and radioisotope. The purpose of which is to provide a reference at drug interactions that could inform nuclear medicine staff in their daily routine. Much of the evidence is based on anecdotal case reports, highlighting the critical importance of adverse event reporting in nuclear medicine. Efforts to increase adverse event reporting, and ideally consolidate reports worldwide, can provide a critically needed resource for prevention of drug-radiopharmaceutical interactions.

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Targeted imaging with ^{64}Cu trastuzumab PET in non-small cell lung cancer

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Introduction: Trastuzumab a humanized monoclonal antibody targets Her2/neu and inhibits neoplastic cell proliferation both in vitro and in vivo and therefore the present study aimed to determine the effect of trastuzumab in Her2/neu expressing non small cell lung cancer (NSCLC) with ^{64}Cu labeled trastuzumab using in vivo PET imaging. **Materials and Methods:** Trastuzumab was conjugated to the bifunctional chelators 1, 4, 7, 10-tetraazacyclododecane-1, 4, 7, 10-tetracetic acid (DOTA) and the in vitro studies were performed to determine the molecular specificity of DOTA-trastuzumab in NSCLC cell line, H2170. DOTA-trastuzumab was radiolabeled with ^{64}Cu for in vivo studies. Imaging of Her2/neu expression was performed with ^{64}Cu -DOTA-trastuzumab in H2170 tumor bearing mouse with PET followed by the biodistribution 1 h, 24 h, and 48 h. **Results:** In vitro studies revealed membranous uptake of DOTA-trastuzumab in the Her2/neu positive H2170 cell line whereas no uptake was seen in Her2/neu negative H520 cell line. Biodistribution and PET studies revealed relatively high accumulation of ^{64}Cu -DOTA-trastuzumab in the Her2/neu overexpressing H2170 tumor at 48h post injection. **Conclusion:** The success of ^{64}Cu -DOTA-trastuzumab brought an insight to PET imaging of Her2/neu gene expression in NSCLC patients with ^{64}Cu -DOTA-trastuzumab to define the patients who might be benefited with trastuzumab based therapy.

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Evaluation of risk of increased cerebral blood flow by intravenous adenosine-tri-phosphate: A PET study with ^{15}O -labeled water.

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Background and Purpose: Adenosine triphosphate (ATP) is well known as a powerful vasodilator and being used for the measurement of coronary flow reserve. However, it has not been investigated whether intravenous ATP could cause significant vasodilation of the cerebral arteries resulting cerebral blood flow (CBF) changes. This positron emission tomography (PET) study investigated the effect of intravenous ATP on human CBF using ^{15}O -labeled water. **Methods:** Ten healthy young male volunteers (age range: 20 to 31 years, mean: 24.0 ± 3.7 years) underwent ^{15}O -labeled water PET scans. The study protocol consisted of baseline, 3 and 1 minute post-ATP intravenous injection studies with dose of 0.16mg/kg/min . CBF images were calculated from dynamic PET data and arterial blood curves

by means of autoradiographic method. Multiple regions of interest were placed and regional CBF values were averaged for each cerebral hemisphere. Statistical parametric mapping (SPM) was also utilized in the data analysis. **Results:** Cortical CBF showed no significant change after ATP administration compared to the baseline (54.0 ± 5.4 at 3 minute and 54.0 ± 6.1 at 1 minute after injection vs. 56.0 ± 5.8 and 56.1 ± 5.4 ml/100g/min at baseline, respectively). Dilatation of major vessels by ATP administration was suggested on SPM analysis, although it did not increase CBF. Heart rates were increased and mean blood pressure was decreased during ATP administration while blood gas data did not show changes. **Conclusion:** The findings indicate that intravenous ATP administration results in dilatation of major cerebral vessels but causes no significant change of CBF due to a decrease in systemic blood pressure.

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Phase I clinical trial and pharmacokinetics of the anti-CEA single chains fragment (scFv)2 M3

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Introduction: The solution to problems like poor tumor penetration, uptake, unhappy pharmacokinetics and a relative high immunogenicity have been encountered by genetic engineering methods, where the multivalent recombinant fragments have become the paradigm of design of constructed molecules for the radio immunotherapy of solid tumor. They are able to retain the parental antibodies specificity and affinity, with reduced immunogenicity and improved pharmacokinetics. The purpose of this study was to evaluate the safety, biodistribution, and pharmacokinetics of the anti-CEA single chains fragment (scFv)2 in patients with colorectal cancer. **Materials and Methods:** This investigation constitutes a Phase I Clinical Trial, where 17 patients were evaluated prospectively. The dimeric structure of the anti-CEA single chains fragment (scFv)2 M3 was attained using antibody engineering techniques in the Center of Genetic Engineering and Biotechnology (CIGB) of Cuba. According to corresponding group, 0.3 or 1 mg of labeled protein with I-131 (activity 185-259 MBq) were injected to patients with colorectal cancer free of onco-specific treatment. Blood and urine samples were measured at different time post administration and analyzed by chromatographic methods. **Results:** In 15 of 17 studied cases the tumor was detected, for a gammagraphic sensibility of 88.2%. Five patients that were tributary to surgery showed a tumor uptake between 3.2×10^{-3} - 16.6×10^{-2} %DI/g. During the study no adverse event was observed, at least related with the clinical trial. The pharmacokinetic data of fragment (scFv)2 M3 was adequately adjusted using a two-compartment open model with mean distribution half-lives of 2.0 and 1.0 hr and mean elimination half-lives of 14.1 and 6.3 hr for the 0.3- and 1-mg groups, respectively. The FPLC analysis showed that the molecule was stable at least for 4h (>88%). From this

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moment begins a label dissociation process, where only a ~ 50% of radioiodine was associated to the protein at 48h - 72h. From the urine samples analysis was concluded that 85% injected activity was excreted through the urine at 72 h post administration, but only the < 2 % of this activity was associated to protein. Conclusions: The results of the Phase I Clinical Trial of the anti-CEA single chains fragment (scFv)₂ M3 labelled with I-131 revealed that the molecule doesn't provoke any adverse event and it is able to recognize its antigen obtaining an tumor uptake of 0.16% ID/g one week post administration. Likewise, the pharmacokinetics studies demonstrated an adequate mean elimination half-life, typical of dimeric fragments. These results promise to be very encouraging for colorectal cancer immunotherapy.

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Experience of radiopharmaceutical therapy in a developing country

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Radiopharmaceuticals are being used in medical diagnosis and therapy for more than half a century. In recent years, with the introduction of many newer radiopharmaceuticals the scope of therapy has been expanded widely. We have seen rapid development of radiopharmaceutical therapy in oncology as well as in non-oncological fields. However, experience of Bangladesh, a developing country, is different. The history of nuclear medicine in Bangladesh is quite old. The first nuclear medicine centre was established back in 1962. Now a total no. of 19 centers including one institute is giving nuclear medicine services in different parts of the country. The institute runs different training programs for physicians as well as for technologists. It also gives post graduate degree in nuclear medicine for nuclear medicine physicians. So far as diagnosis is concerned, the country has progressed up to a level. Almost all the centers have SPECT gamma cameras. Some of the centers have acquired SPECT-CT. The institute is expecting PET-CT in year 2011. A wide range of diagnostic procedures including thyroid, bone, kidney, cardiac and neurological studies are done routinely in almost all the centers; thyroid study being in the top of the list. However the picture is different in therapy field. Still the country is mainly doing I-131 therapy for treatment of thyrotoxicosis and thyroid cancer. Besides the country has an experience of P-32 therapy for myeloproliferative disorder like polycythemia vera or occasional use of radiocolloids for radiosynovectomy. When the developed countries are using radioisotopes like Strontium-89, Samarium-153, Rhenium-188 or Iodine - 131 MIBG in routine therapy, Bangladesh is still fighting for I-131 iodide capsule or liquid for thyroid cancer or thyrotoxicosis therapy. The only 3 MW research reactor of the country can not meet the demand of the patients. The country is dependent on a third country for its total demand. And that is a big story. Many a times the supply is not in time and sometimes the whole lot is cancelled for many reasons. This brings great suffering of the patients especially the cancer thyroid patients who are waiting in hypothyroid condition for I-131 therapy. The country is far away from

procuring Sr-89, Sm-153 or other radioisotopes which are much more costly. The world nuclear medicine community especially the World Radiopharmaceutical Therapy Council is working its best for promotion and development of radiopharmaceutical therapy for the last couple of years. Time has come that it should ensure the homogeneous growth of radiopharmaceutical therapy throughout the world.