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DHARAMSHILA HOSPITAL
YOUR PARTNER IN CANCER CARE

DHARAMSHILA HOSPITAL AND RESEARCH CENTRE
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Dharamshila Marg, Vasundhara Enclave, Delhi 110096

FACILITIES AVAILABLE

DIAGNOSTIC SERVICES

Radiology and Imaging Services
- PET CT Scanner with HD Technology
- Gamma Camera for Nuclear Scans
- 16 Slice Multi Detector CT Scanner
- 1.5 Tesla Magnetic Resonance Imaging (MRI)
- Mammography
- Ultra Sonography Scans
- Colour Doppler Vascular & Cardiac Studies
- CT /USG guided interventions
- Image intensifier – C-Arm
- Digital Radiography
- Interventional Radiology

Cardiopulmonary Lab
- ECG - Holter Test - TMT, PFT
- Stress/Dobutamine Echo with Colour Doppler

Laboratory Services
- Histopathology - Haematology
- Cytopathology - Biochemistry
- FNAC & Guided FNAC - Clinical pathology
- Frozen Section - Microbiology
- Immunohistochemistry
- Tumour Markers
- Cytochemistry
- Serology
- 24X7 Blood Bank with Apheresis and Blood Components facility

Endoscopic Suite – Full Range of Fibre-optic
Endoscopic Procedures

RADIATION ONCOLOGY
- Triple energy Linear Accelerator with Volumetric Arc Therapy (VMAT)
- IGRT, IMRT, 3D Conformal Treatment
- Stereotactic Body Radiation Therapy (SBRT)
- Stereotactic Radio Surgery (SRS) and
- Stereotactic Radio Therapy (SRT)

MicroSelectron Digital (HDR-V3) Brachytherapy Afterloader Intracavitary, Interstitial, Intra luminal and Surface mould

Treatment Planning Systems
(Eclipse, CMS Xio, Monaco, ERGO++, Plato Sunrise)

SURGICAL ONCOLOGY
- Head and Neck Cancer Surgery
- Esophageal Cancer Surgery
- Breast Cancer Surgery
- Chest & Thorax Cancer Surgery
- Gynae Cancer Surgery
- Gastrointestinal Cancer Surgery
- Uro oncology surgery
- Neuro oncology Surgery
- Bone and Soft Tissue

MEDICAL ONCOLOGY

Chemotherapy Normal & High Dose Including
- Infusional Chemotherapy
- Targeted Therapy
- Immunotherapy / Biological Therapy
- Hormonal Therapy
- Site Specific Chemotherapy

HAEMATO ONCOLOGY (ADULT & CHILDREN)

State-of-the-art Blood And Marrow Transplant Centre
- Autologus BMT for Myeloma, Lymphoma, Paediatric tumours, Multiple Sclerosis and Auto-immune disease, not responding to the medical treatment.
- Allogenic BMT for Acute Leukemia, Chronic Leukemia, Lymphoma, Myeloma, Thalassemia, Sickle cell disease, Childhood genetic diseases, Immunodeficiency, Metabolic diseases, Solid Tumours and Auto-immune disease not responding to the medical treatment.
- Non-Malignant Hematology services to cater to patients with Thalassemia, Aplastic Anemia and others
- Excellent Blood bank facilities for Collection, Processing, enumeration and Cryopreservation of stem cells. BMT Labs are equipped with state-of-the-art equipments for Routine and Specialized Tests. HLA Testing, Bacterial and fungal cultures, Flow Cytometery, Conventional and Real Time PCR for viral pathogens, Molecular Biology Lab, Cell Culture Lab and Magnetic separation of cells using MACS technology.

ALLIED SPECIALITIES

Superspecialities
- Gastroenterology & Gastro-intestinal Surgery
- Nephrology – Dialysis
- Neuro Surgery
- Plastic and Cosmetic Surgery
- Pulmonology
- Urology

Specialities
- Dental
- Ear, Nose and Throat (ENT)
- General and Laparoscopic Surgery
- Gynaecology
- Internal medicine
- Orthopaedics (Joint Replacements)
- Rehabilitation & Speech Therapy

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DHARAMSHILA HOSPITAL
YOUR PARTNER IN CANCER CARE

DHARAMSHILA 23 years Adding quality to life

Dear friends,

With the onset of the summer the work load has increased and so have our success rates of Bone Marrow Transplantation. The enrolment of children requiring Haploidentical BMT is in full swing. Our BMT website is operational, for any queries regarding BMT, please visit our website ***www.bmthospitalindia.com***

Due to lack of awareness and delayed diagnosis, majority of patients lose their precious lives. This can be prevented by public awareness and CME programmes. As part of Continuous Medical Education programmes, we organize monthly CME Programme on Sundays from 10 a.m to 2 p.m. Each CME covers latest techniques for early diagnosis and management of Breast, Head and Neck Gastrointestinal, Gyanecological and Haematological malignancies. In case your organisation/IMA/Association is interested, kindly do let us know the suitable date.

We have also started ***Dharamshila Multispeciality Centre****, a 50 bedded facility for our neighbours, attendants and comprehensive treatment of our cancer patients with associated diseases.*

We have also become the chosen destination for specialised lab tests, MRI, PET CT, CT, Nuclear Scans etc, we also provide leukodepleted blood, irradiated blood and blood products, single donor platelets to our neighbourhood hospitals. Details of our diagnostic facilities are listed on the back cover page.

\We are considering replacing DCFRC Newsletter with E-newsletter. Those of you who are interested, please do send your e-mail address so that we put you on our mailing list for DCFRC E-newsletter.

Looking forward for your valuable support

Thanking you

Dr. S. Khanna
President, DCFRC

ADAPTIVE IMAGE GUIDED BRACHYTHERAPY IN CARCINOMA CERVIX.....THE NEW BUZZ

Despite major advances in technology, the treatment outcomes in carcinoma cervix did not improve significantly for many decades. The concept of "see what you treat" has slowly percolated in brachytherapy procedures by incorporation of Magnetic resonance imaging (MRI) in brachytherapy planning. With the advent of high dose rate (HDR) equipment and integration with Image guided 3D dose optimisation, improvement in local control is possible.

MRI is nowadays considered the gold standard for 3D image guided adaptive cervix cancer brachytherapy as it provides detailed anatomical information for application and treatment planning. MRI based brachytherapy (BT) allows appropriate delineation of target volumes for brachytherapy treatment planning. Proper dose shaping, i.e., escalating the dose for MRI based target volumes (High risk clinical target volume) while keeping it reasonably low for organs at risk (OAR), seems to be the major factor in successfully improving local control and minimizing late side effects. This target based dose escalation has helped in improvement of local control in carcinoma cervix.

There is evidence that the use of computed tomography (CT) only for brachytherapy target volume definition is inferior to MRI and introduces major uncertainties in dose assessment and therefore optimal dose planning. However, the use of an MRI for brachytherapy with the applicator in place is difficult to organize and is expensive

Prerequisites

Technical requirements for commissioning image guided brachytherapy (MRI based) are as follows:

• MRI compatible brachytherapy applicators

The conventional metallic brachytherapy applicators cannot be used due to possibility of image distortion, heating and mechanical tissue injuries. Specialised MRI compatible applicators are required. Non-metallic (e.g. plastic) and titanium applicators do not interfere with

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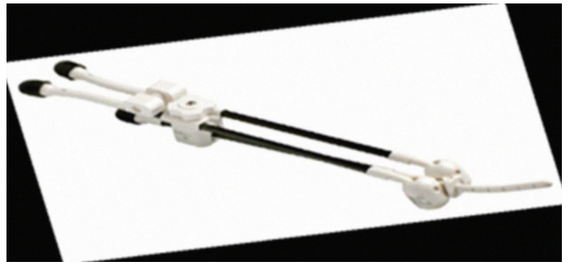
the magnetic field, and they appear as black voids in the images.



Pic 1: MRI Compatible applicator at DHRC

• Magnet field strength

Both low (0.1–0.5 Tesla) and high 1.0–1.5 T field imagers conform to the requirements of ''Brachytherapy MRI examination''. Strength of 3T or higher as in diagnostic radiology have issues of image distortion, artefacts and potential magnet configuration.

• Co-ordination

A close coordination between radiation oncology and radiology department is required. The patient with brachytherapy applicator has to be prioritised over the patients to minimise the applicator displacements. The MRI technologist has to be well versed with the parameters of scan acquisition for brachytherapy planning. Inputs from the radiologists in target delineation are essential unless and until there is thorough understanding of MRI.

• Appropriate planning Software

Patient preparation

To derive maximal information from the MRI study-patient preparation is a vital step. To conform to the requirements of BT intervention and MR imaging, bowel preparation is started 2 days prior to the intervention. To reduce bowel motion, intravenous or intramuscular antispasmodic drug administration should be considered. MR image quality can be further improved by reducing the anterior abdominal wall motion amplitude with a large elastic band. Intravaginal application of intermediate-to-high signal intensity contrast-media (like ultrasound gelly) for pre radiation MRI examination unfolds the vaginal fornices thus revealing signs of invasion and exophytic tumour growth. It is also recommended to apply dedicated bladder filling protocols in order to achieve reproducible bladder filling during image acquisition and BT delivery.

BT MRI Examination and Interpretation

After the placement of the applicator on T2-weighted sequences, MRI-compatible applicators and MRI-compatible interstitial titanium or plastic needles are depicted with low-signal intensity and with sufficient contrast to the adjacent patho-anatomical structures, which are displayed with intermediate to high signal intensity. The vaginal packing used for the stabilisation of the applicator and to displace the rectum and the bladder from the intravaginal parts of the applicator, can be impregnated with diluted gadolinium contrast agent or can be left dry (in 1.5 T). This ensures improved discrimination quality for the delineation of the lower parts of the cervix/tumour

• Imaging parameters

Parameters as proposed by GEC-ESTRO are helpful in improving image acquisition.

Target and OAR Delineation

It is important to have image plane orientation and understanding of MRI anatomy. High risk clinical target volume (HR-CTV) for BT carrying a high tumour load, includes always the whole cervix and the presumed extracervical tumour extension at the time of BT.

Intermediate risk CTV (IRCTV) includes a significant microscopic tumour load, encompasses high risk CTV1 with a safety margin of 5–15 mm. Amount of safety margin is chosen according to tumour size and location, potential tumour spread, tumour regression and treatment strategy.

Imaging and applicator reconstruction

Special MRI markers like catheters containing water, CuSo4 solution or glycerine are alternatives that can be used to guide the reconstruction of catheters. It is advisable to practice catheter reconstruction prior to a definite plan.

Planning and Reporting

Cumulative dose volume histograms (DVH) are recommended for evaluation of the complex dose heterogeneity. DVH parameters for GTV, HR CTV and IR CTV are recorded as per Table 1 .

Table 1
Recommendations for recoding and reporting 3D gynaecological brachytherapy

- Complete description of clinical situation including anatomy and pathology and imaging.
- Examination dimensions and volume of GTV at diagnosis and at time of brachytherapy.
- Dimensions and volumes of HR CTV and IR CTV, respectively.
- Complete description of 3D sectional imaging technique and contouring procedure.
- Complete description of brachytherapy technique radionuclide; source type (wire, stepping source); source strength; applicator type' type o after loading (manual or remote); description of additional interstitial needles if any.
- Treatment prescription and treatment planning applicator reconstruction technique, standard loading pattern, dose specification method' optimization method, if applied
- Prescribed dose:-

Total Reference Air Kerma (TRAK)
Dose at point A (right, left, mean)
D100, D90 for GTV & HR CTV and IR CTV, respectively.
Dose to bladder and rectum for ICRU reference points $D_{.1cc}$, D_{1cc}, D_{2cc} for organs at risk (e.g rectum, sigmoid, bladder) (vagina[a])
D_{5cc}, D_{1cc}, D_{2cc} for organs if contouring of organ walls is performed
Complete description of time dose pattern: physical and biologically weighted doses (α / β = 10 Gy for GTV and CTV and α / β=3 Gy for OAR; $T_{1/2}$ = 1.5 h for GTV, CTV and OAR)

For vagina dose volume parameters still need to be defined.

Logistics

Since MRI is not available for planning of each BT fraction in all institutions where image guided cervix cancer BT is performed, studies combining MRI and CT for different fractions have been reported in the literature. They have shown that a combination of MRI for first fraction and subsequent CT based planning is feasible as well as quick and easy when automatic applicator-based image registration and target transfer are implemented in the TPS. The results show striking similarity to fully MRI-based planning in cases of small tumours and intracavitary applications, both in terms of HR CTV coverage and respecting of OAR dose limits. The MRI/CT combination method may further be improved by focussing on information from clinical examination in the CT-based planning process and better understanding of CT contouring.

The MRI based HR CTV contour for the first fraction can be used as an appropriate surrogate for the HR CTV to be used when subsequent fractions are scanned with CT for treatment planning.

The applicator and the HR CTV are linked together in a reproducible way. This implies that after re-insertion of an identical tandem/ring applicator the geometrical relation between HR CTV and applicator will be the same.

However, this is not true for larger tumours and complex applications, as well as situations with unfavourable OAR topography, especially for the sigmoid; where MRI based adaptive BT planning remains the superior method and is hence still to be considered as the gold standard.

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THE SUCCESS STORY OF ALLOGENEIC BMT: THE GLASS IS ALWAYS HALF FULL

The Great Beginning

Allogeneic BMT had attracted the researchers for over half a century and led to over 200 attempts at bone marrow transplantation in human subjects by 1960. However, a review of all such cases revealed that not a single one was successful and most had resigned to the fact that it was a part of medical fantasy which never came to reality. But over the ages mankind has progressed as some have had the faith and conviction to swim against the tide. ED Thomas who had just moved to FHCRC, Seattle around the same time had different ideas. He and his colleagues spend a decade in painstaking basic research on canine subjects to demystify the art and science of BMT. ED Thomas did his first BMT in a patient with end stage leukemia in 1969 and 42 years later he passed away witnessing a million bone marrow transplants being performed.

A Long Road Travelled & A Long Road To Go

With a million transplants in our bag, only a handful of patients in India can actually get a BMT when needed. The premises of a successful BMT are based on perfect matching of HLA antigens between the patient and the donor. Such a perfect donor is usually a first degree relative but is available to about 20% of the patients. The conserved Caucasian gene pool allows 80% of patients without a matched family donor to avail one from the Volunteer Unrelated Donor Registries. Even for those without a Matched Unrelated Donor, Public Cord Blood banks can provide an option for BMT. Thus, in the western world, rarely does one end up not having a BMT due to the lack of a Matched family Donor.

In India, the estimated number of patients needing a BMT is over 30,000. And yet, only about 1000 patients get a transplant. The major cause lies in the lack of alternate donors. The chance of finding a match for an Indian from a foreign VUD registry is less than 10% and the cost of procuring one is anywhere between 30-40,000 USD at the minimum. The same holds true for Unrelated Cord Blood Units.

Nature shows the way

The saying that "nature is the mother of all inventions" is not without reason. HLA antigens are inherited as a set from each of the parents. A mother nurtures a baby in her womb for 9 months without rejecting it even though the paternal HLA antigens inherited by the baby should cause a rejection. This is nature's example of development of tolerance and thus, a child and the mother are natural donors for each other in most cases even though they are only half matched in their HLA antigens. Based on the pioneering work by doctors from Italy, BMT from a half matched **(Haploidentical)** donor from the family was developed. Yet, it was challenging and often not reproducible. The researchers from Johns Hopkins and FHCRC, Seattle innovated yet another way of carrying out Haploidentical BMT which was more reproducible.

Everyone has a donor!!!

In a country where alternate donor BMT is rarely available for patients lacking a matched family donor, Haploidentical BMT seems to be a logical option. However, the lack of expertise and infrastructure halted its development. **Dr. SuparnoChakrabarti** and **Dr. Sarita Jaiswal** pioneered the first Haploidentical BMT program in India. Their work and research has been widely presented and published in the last two years. Having performed over 30 such transplants, they wanted to develop this procedure further. **Dr. Sarita Jaiswal** trained under **Prof. Franco Aversa** from Italy, who is the pioneer of Haploidentical BMT. Prof Aversa and others have developed a completely new approach to Haploidentical BMT using **Clinimacs** based depletion of TCRalfabeta and CD19 cells from the stem cell product, which has drastically reduced the rate of complications and mortality experienced earlier. This is a labour intensive technology and carrying out such transplants without the right expertise or infrastructure can be disastrous. The experience at University of Parma under Prof Aversa amazed Dr Sarita as to how well such transplants can be carried out with the right expertise if a supportive infrastructure is provided. **At the same time, the method of Haploidentical BMT pioneered by Dr.SuparnoChakrbarti is equally applicable to most patients.**

CliniMACS based Haploidentical BMT Program at Dharamshila Hospital.

As Dharamshila BMT centre has the right expertise and technology to develop this Haploidentical program for the first time in India, this might be the right step forward for children with **Leukemia, Thalassemia and Aplastic Anemia** without matched family donors. **This program has been initiated for children with these diseases and enrolment has started.** Subsequently, this shall be extended to the adult patients.

For further information, please visit our website
www.bmthospitalindia.com

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