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DHARAMSHILA HOSPITAL AND RESEARCH CENTRE

(A unit of Dharamshila Cancer Foundation And Research Centre)

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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)
 - MicroSelection Digital (HDR-V3) Brachytherapy Afterloader Intracavitary, Interstitial, Intra luminal and Surface mould
 Treatment Planning Systems
 (Eclipse, CMS Xio, Monaco, ERGO++, Plato SURTE)

SURGICAL ONCOLOGY

- Head and Neck Cancer Surgery
 - Esophageal Cancer Surgery
 - Breast Cancer Surgery
 - Chest & Thorax Cancer Surgery
 - Gynaec 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
 - Autologous 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 Cytometry, 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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Dear friends,

It gives me immense pleasure to share with you that Dharamshila Hospital And Research Centre has received three awards in the month of July.

On 1st July 2014, Doctor's Day, Dharamshila Hospital And Research Centre received IMA Medachiever's.com Award from Dr. Harsh Vardhan, Union Minister of Health and Family Welfare for "DHARAMSHILA'S CONTRIBUTION TO PROGRESS IN ONCOLOGY IN INDIA". We were shortlisted by an eminent National jury, consisting of stalwarts from Medical Council of India, National Board of Examination, NABH, Secretary General IMA and others.

On 19th July 2014, we received two other awards from India Leadership Conclave 2014 and India Affairs Business Leadership. The 1st Award was for India's Most Promising Health Care Centre 2014 and the second was awarded to our CEO, Dr. Sandeep Chatrath as "CEO of the year – Healthcare".

On 26th July 2014 we were judged by the real judges "OUR CANCER SURVIVORS" They judged us as the MOST TECHNICALLY ADVANCED, ETHICAL, ECONOMICAL AND PATIENT FRIENDLY HOSPITAL. We had organised a meeting with our cancer survivors in collaboration with Rotary Club, Shahdara. They shared their journey from being a cancer patient to a winner with each other and the care providers. These awards and recognitions reflect Dharamshila's rising popularity as a leading cancer hospital of India which has changed the scene of cancer not only in North India but the entire country.

We went through second reassessment for NABL Accreditation ISO 15189, 2012 and NABL 112 on 19th and 20th July 2014 and our NABL Accreditation is continued.

We organized a workshop on Advanced Cardiac Life Support (ACLS) and Basic Life Support (BLS) on 25th, 26th and 27th July 2014 at Dharamshila Hospital And Research Centre, Nodal Centre of Maulana Azad Medical College, Delhi. Total 31 Participants (Doctors, Nurses, Technicians, Physiotherapists, etc) from the hospitals of Delhi / NCR, Haryana & U. P. attended the workshop and successfully completed the course.

Dr. S. Khanna
 President, DCFRC

TREATMENT OF METASTATIC RENAL CELL CARCINOMA IN 2014

The overall survival of the patients with metastatic renal cell carcinoma has improved substantially in the last decade thanks to the new molecular targeted, anti-angiogenic, and immunotherapeutic agents. From Interferon and Interleukin-2, targeted agents have become the standard of care in this disease. The median overall survival was increased to 26.4 months when first-line sunitinib was used compared to Interferon alpha. Objective response rate was 47% for sunitinib compared with 12% for IFN-alpha.

We still do not know the ideal sequence of the targeted agents or whether one sequence is more promising than the another. Currently there is a thought that the sequence of the agents does not matter at all if the patient has favourable prognostic features and has got access to all targeted agents in his lifetime.

Is there an advantage of removing the primary tumour in metastatic RCC?

A combined analysis of 2 previous trials demonstrated an overall survival advantage for the cytoreductive nephrectomy (CN) (13.6 months survival with CN versus 7.8 months for the Interferon alone arm) when metastatic RCC was treated with or without CN followed by IFN alpha. Till date, the benefit of CN in the targeted therapy era has been only shown with retrospective reports, and has yet to be proven in prospective trials.

The SURTIME trial (NCT01099423) is currently planning to randomize 458 patients to either CN followed by Sunitinib (immediate nephrectomy) or Sunitinib then CN (delayed nephrectomy) followed by additional Sunitinib, with progression-free survival as the primary outcome. The CARMENA trial (NCT00930033) is randomizing an estimated 576 patients to receiving Sunitinib only (with no CN to follow) or to undergo CN followed by Sunitinib, with OS as primary endpoint.

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India's First NABH Accredited Cancer Hospital | Laboratory Services Accredited by NABL
 ISO 9001:2008 and ISO 14001:2004 Certified by TUV - NORD, Germany

What about resection of metastasis?

Resection of metastases is to be performed whenever complete resection appeared feasible. Some small series have demonstrated the benefits of even incomplete metastasectomy—but careful patient selection is important. But patients with upfront solitary metastasis (especially lung, bone and brain) and those developing solitary metastatic recurrence after prolonged disease free interval are ideal candidates.

What are the first-line agents in metastatic RCC?

Targeted therapy with tyrosine kinase inhibitors are currently the drugs of choice in the first and second line treatment in metastatic RCC. High dose IL-2 therapy, as it can cause long-lasting complete remission in a small subset of metastatic RCC remains a treatment option in highly selected patients (clear cell, no medical comorbidities and patient willing to take high risk).

Broadly metastatic RCC can be divided into good, intermediate risk and poor risk based on a prognostic factor model consisting of 6 factors (LDH, hemoglobin, corrected serum calcium, interval of less than 1 year from diagnosis to start of systemic treatment, Karnowsky performance status less/equal to 70, 2 or more sites of metastasis), Patients with 3 or more factors are considered poor risk and is a candidate for upfront Temozolomide (mTOR inhibitor). The median overall survival was 10.9 Vs 7.3 months when Temozolomide was compared with IFN alpha.

Sunitinib, Pazopanib and Bevacizumab plus Interferon alpha are the currently approved first-line agents in metastatic RCC.

In the pivotal trial, the median PFS was 11 months for the Sunitinib compared to 5 months for IFN alpha. The overall survival was 26.4 months Vs 21.81 months. COMPARZ is a large non-inferiority trial of Sunitinib versus Pazopanib. This study showed Pazopanib has similar efficacy but less toxicity compared to Sunitinib. Bevacizumab plus IFN alpha was compared with IFN alpha in a large multi-centre Phase 3 trial (AVOREN). The median PFS was 10.2 months Vs 5.4 months and the median OS was 23.3 months Vs 21.3 months favoring the Bevacizumab plus IFN alpha arm.

What are the second-line agents in metastatic RCC after frontline TKI ?

It appears that there is no absolute cross-resistance on occurrence of resistance to the first-line TKI. Axitinib and Everolimus, both have the highest level of recommendation for use after failure of first-line targeted agents.

Axitinib-Based on the AXIS trial results, Axitinib was approved for second-line treatment after failure of Sunitinib or cytokines. Patients who had progressed on Sunitinib, cytokines, Temozolomide or Bevacizumab were randomly assigned to receive Axitinib or Sorafenib. The median PFS was significantly longer with Axitinib compared with Sorafenib (6.7 months vs. 4.7 months; HR 0.665; 95% CI 0.544–0.812; p < 0.0001).

Everolimus- Everolimus was the first agent to receive approval for second-line treatment after tyrosine kinase inhibitor (TKI) failure. Approval was

based on the observation in the RECORD-1 trial that patients assigned to Everolimus had a significantly longer PFS than those on placebo (4.9 vs. 1.9 months)

Sorafenib-Based on INTORSECT trial, patients who had progressed on Sunitinib were randomly assigned to Sorafenib (VEGFR-TKI) or Temozolomide (mTOR inhibitor), with PFS as the primary study endpoint. No statistically significant difference was found between treatment arms with regard to PFS (Temozolomide: 4.28 months; 95% CI 4.01–5.43; Sorafenib: 3.91 months; 95% CI 2.80–4.21), but OS was significantly longer for patients assigned to Sorafenib when compared with Temozolomide (Sorafenib: 16.64 months; 95% CI 13.55–18.72; Temozolomide: 12.27 months; 95% CI 10.13–14.80; p = 0.014).

Is continuous treatment till progression really important?

As per today the accepted strategy is to extract the maximum benefit from each treatment line as fewer patients are going to the second- or third-line treatment. It is questionable whether continuous treatment exposure until progression is really important. Rini et al demonstrated that Sunitinib dosing with periods of drug-free interval is associated with a reduction of side effects without compromising clinical efficacy. Time off drug allows resetting of the tumor microenvironment and maintaining sensitivity to VEGF inhibition.

Another strategy is using alternating agents with different modes of action before resistance occurs. The SUNRISES study (NCT01784978) is investigating alternating cycles of Sunitinib and Everolimus compared with sequential treatment of Sunitinib followed by Everolimus on progression. The average life of Metastatic RCC in 2014 is a little above 2 years and has reached a plateau. More new agents and more insight into the resistance mechanism of existing agents are the need of the hour.

Dr. K. M. Parthasarathy

MD, DM, ECOMO

Senior Consultant, Medical Oncology

PERINEAL INTERSTITIAL BRACHYTHERAPY IN RECURRENT CARCINOMA CERVIX

Interstitial Brachytherapy is a form of brachytherapy where sealed radioactive sources are directly implanted surgically into the tumor in a geometric fashion. In gynaecological malignancies, it is used in the following settings:

1. Ca Cervix IB, II B & above if
 - a) Anatomy is distorted
 - b) Narrow vagina and obliterated fornices
 - c) Os / Uterine canal not identifiable
2. Extensive paravaginal (>0.5cm) or distal vaginal involvement
3. Bulky parametrial disease which will require boost.
4. Persistent or Recurrent Ca Cx post EBRT +- ICA.

5. Carcinoma of the cervical stump, Cut through hysterectomy.
6. Post operative vault recurrence
7. Ca Endometrium - Local recurrence Post Sx +- RT extending beyond the confines of vaginal vault (not extending to the pelvic wall)
8. Vagina and Vulva

Radical Brachytherapy in early lesions (T1/N0)

Boost in addition to external beam radiotherapy in large lesions (T2/3).

Locally confined recurrent cases.



Different templates were designed in order to get a better target volume coverage. The gynaecological applicators / templates are: Syed Neblett applicator, Martinez

Universal Perineal Interstitial template (MUPIT), Vienna applicator, Hammersmith Hedge Hog & Queen Mary Hospital Applicator. At our centre we use MUPIT. Cases of recurrent carcinoma of cervix are difficult to treat. Options include radiation therapy in radiation naive patients, pelvic exenteration and interstitial Brachytherapy. Since majority of non metastatic cervical cancers are primarily treated by radiation therapy (with/without concurrent chemotherapy), the choice is between the exenteration (which is a morbid modality) and interstitial brachytherapy. Although no randomized comparisons have been done between the two in this setting, available data suggests local control of the order of 50% - 80% at 5 years across different authors in case of interstitial brachytherapy with a reasonable rate of complications and around 17%-20% requiring salvage surgery even then

Main results with interstitial brachytherapy:

AUTHOR	IMPLANT SYSTEM	PATIENT NUMBER	LOCALISATION	PRIMARY(P) RECURRENT(R)	LOCAL CONTROL	SURVIVAL	COMPLICATION
CHARRA (11)	INTRA VAGINAL TEMPLATE	78	CERVIX: 41 ENDOMETRIUM: 37	R	AT 5 YEARS 70.4%	AT 5 YEARS OS: 56 % SS: 62 % DFS: 51 %	16 % GRADE 3: 10.2 %
MARTINEZ (9)	MUPIT	35	CERVIX: 5 URETHRA: 6 ANUS: 7 VAGINA: 8 VULVA: 9	P + R	88 %		GRADE 1-2:15/35 GRADE 3: 2/35
MARTINEZ (28)	MUPIT	104	CERVIX URETHRA PROSTATE VAGINA ANORECTAL	P + R	83.8 %		GRADE 3:4/104
GUPTA (24)	MUPIT 24 PTS WITH INTERSTITIAL HYPERHERMIA	69	CERVIX URETHRA ENDOMETRIUM VAGINA	P + R	AT 3 YEARS 80 % P: 50 % R: 88 %	AT 3 YEARS OS: 41 % DFS: 55 %	GRADE 4:14 %
ARISTIXABAL (29,30)	SYED - NEBLETT TEMPLATE	106	CERVIX	P	MEAN FU: 23 MONTHS 75 %		GRADE 2-3:18 %
HUGHES DAVIES(32)	MUPIT	139	CERVIX: 93 ENDOMETRIUM: 14 RECTUM: 6 PALLIATIVE: 5 VAGINA: 20 VULVA: 20	P + R	MEAN FU: 57 MONTHS AT 5 YEARS 25 %	AT 5 YEARS OS: 35 % DFS: 32 %	REQUIRING SURGERY: 17 %
HALE - MEDER(31)	GG, PT, SYED - NEBLETT TEMPLATE	150	CERVIX URETHRA VULVA VAGINA	P: 101 R: 49	AT 5 YEARS: 80 %	AT 5 YEARS OS: 35 % DFS: 30 %	GRADE 3-4: 11/135

Most of the results in literature are from centres practicing low dose rate brachytherapy, where the complication rates and procedure related morbidity are deemed higher. At our centre we have high dose rate brachytherapy system which has the following benefits:

- No long confinement to bed for the patient

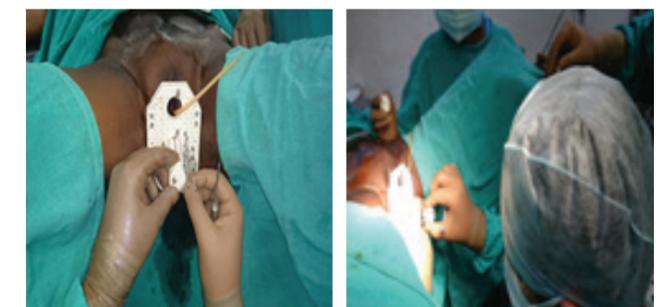
- No indwelling bladder catheters for prolonged times
- Not labeled "radiation risk zone" to relatives, visitors and staff
- Brief treatment times – position of sources maintained
- No specialized nursing
- Ability to treat larger number of patients
- Shorter treatment times & minimal radiation protection problems
- Image guided and image based planning
- Possibility of optimizing dose distribution by altering the dwell times of the single stepping source at different dwell positions

However, experience with high dose rate brachytherapy is relatively new and fewer centres have the capital and the expertise required to practice it. At DHRC, we do a significant number of cases routinely and we have a good number of successfully treated patients.

Perineal interstitial Brachytherapy is a very gratifying modality but it requires a certain degree of expertise – both in the surgical placement of applicators as well as optimization and planning.

At our centre the cases are carefully selected based on the locoregional clinical findings and imaging (MRI). A pre-treatment tumor mapping is done and the entire procedure is planned. The procedure itself is done under spinal/epidural anaesthesia. The positioning of applicators through the template is done under TRUS guidance. After the application, a CT scan is done and the images are transferred to the planning system. Organs at risk and the target tumor are carefully delineated; and optimization is done to achieve the clinical objectives. After the procedure, the applicators are removed and hemostasis is achieved. The procedure is repeated for a total of 2-3 sittings, a week apart. The complications are those related to GA/ spinal anaesthesia, bleeding, bladder or rectal discomfort and dull pelvic pain which are usually manageable.

Hopefully perineal interstitial brachytherapy will be one of the options for this subgroup of cervix patients where usually there is not much to offer and palliation is the usual call.



Dr. Manish Bhushan Pandey

Consultant (Radiation Oncology)

MD, DNB (Radiation Oncology)

Experienced in IMRT Based Total Marrow and Lymphoid Irradiation for BMT