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# KMCH Touch

Quarterly News Journal of Kovai Medical Center and Hospital

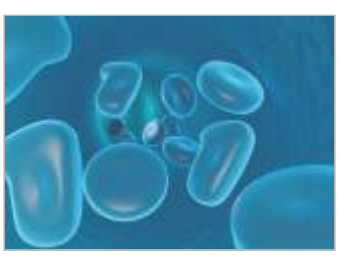
EXCELLENCE IN HEALTH CARE 28 1990 - 2018 KMCH

## The Future of Cancer Therapy:

## KMCH is launching India's First TruBEAM with Hyperarc

Also Articles on

Is Our Fear of HRT side effects leaving women behind



Immunotherapy & Targeted Therapy

Theragnostics & PET guided Biopsies

Novel Delivery of Intraperitoneal Chemotherapy For Ovarian Cancer

## Message From Executive Director

**The Future of Cancer Therapy**

Greetings everyone ! We are making changes to the KMCH touch to make it more friendly to the doctor community . We have tried 3 things this issue

(1) I would like to use this opportunity congratulate our oncology team for their hard work for getting their 2nd Linear accelerator . The new Linear machine , Varian TruBEAM with Hyperarc will be the 2nd Hyperarc facility in Asia and the 1st in India. KMCH is trying to keep itself on the forefront of cancer care . From robotic surgery for prostate cancer and esophageal cancer to the latest in immunotherapy and targeted therapy to Onco-pathology and Genetics lab to HIPEC & EPIC, we have come a long way and we can definitely say that Coimbatore offers some of the best cancer care in the country. Still if you ask Coimbatore oncologists, we still lose out to alternate therapy providers , scared patients who don't follow up , and patients going to Major metros to find the better facilities ( and sometimes pay much more and get worse care) . We have patients go to CMC Vellore and Tata Memorial for immunotherapy and targeted therapy thinking only these centers offer these therapies and to their surprise they are asked to follow and continue care with us.

(2) We are also introducing a quarterly Women's Health Corner in this issue.

(3) We have also decided to share with the medical community our Antibiogram data . We have always emphasized responsible antibiotic use. So we thought it is best to share the antibiogram data so our community has the information first hand and will supply them with latest treatment guidelines as needed.

*"Never be ashamed of a scar*

*It simply means you were stronger than whatever tried to hurt you. "*

**Dr Arun N Palaniswami**
Executive Director

## Editorial Board

There is a beautiful line in Robin's Textbook of Pathology about cancer.

"The only way not to get cancer is not be born, to be born is to incur the risk". However, we have come miles ahead in Cancer diagnostics and Therapeutics over the last two decades. At KMCH, we are extremely proud of our multi-disciplinary Oncology services with the state of the art technology in combination with a great touch of humanity. This Edition is dedicated to our Oncology team who strive hard to make our patients lives better everyday. I hope all of us learn from this issue.

As usual, kindly send any feedback to drkrishnanswaminathan@kmchhospitals.com

**Dr. Krishnan Swaminathan** MD FRCP (Edin)

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*Dr. J. Sivakumaran - Chief Operating Officer, receives Economic Times Business Excellence Award from Thiru. K.Pandiarajan, Minister for Tamil Official Language & Tamil Culture*

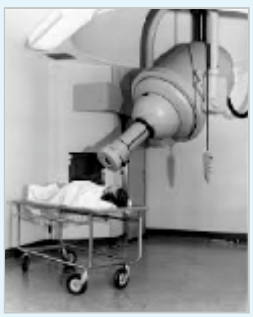

*Mr. Ravindrakumar - Chief Financial Officer, receives Best CFO of Year 2019 Award by Financial Express*

# History of Radiotherapy

History of Radiotherapy: From its humble beginning as radium treatment, modern radiotherapy has come a long way.

Radium Era (1895 - 1930): The discovery of X-rays in 1895 by Wilhelm Conrad Roentgen was the first breakthrough on the use of ionising beams. Before understanding the physical properties of X-rays and their biological effects, Emil Herman Grubbe used x-rays to treat a patient with breast cancer in 1896. In the same year, Antoine Henri Becquerel started to study the phenomenon of radioactivity and in 1898, Maria Sklodowska-Curie and her husband Pierre Curie discovered radium as a source of radiation. In 1901, Becquerel and Curie reported on the physiological effects of radium rays. Skin cancers were the most frequently treated, because of the low depth penetration of the radiation beam. In 1910, Coolidge developed a new device to emit high energy x-rays to treat deep seated cancers. In reality, due to lack of knowledge on the mechanism & properties of radiation beams, the results were poor in comparison to the side-effects.

Orthovoltage Era (1930 - 1950): This time period was characterised by the use of the radium-based interstitial irradiation (brachytherapy) and by the development of supervoltage X-ray tubes able to deliver energy from 50 kV to 200 kV to treat skin lesions & superficial tumours. Things continued to evolve when scientists began to understand the nature of radiation, their modalities of action and their relationship between time and dose of radiation on cell survival. The concept of fractionated radiotherapy was introduced in 1935 to maximise tumour control and reduce side-effects.



Megavoltage Era (1950 - 1990): This period saw the introduction of the Cobalt teletherapy which used the reactor-produced isotope cobalt 60 (60Co) to generate gamma rays of about 1.25 MeV, arrived on the scene producing high-energy γ-rays. The new device had the ability to treat deep seated tumours with a greater skin sparing. Radiotherapy practices in this era incorporated the use of anatomical landmarks as well as radiological correlation with 2D-imaging in the form of port films or fluoroscopic imaging. Multifield radiation treatment plans were also designed.

## Current Era

Current radiation therapy is routinely delivered using a linear accelerator( Linac) and traces its origins to the invention of the "klystron" tube by brothers Russell and Sigurd Varian in 1937. It underwent a series of technical transformation allowing us to regulate the dose precisely and serve as a platform for today's advanced radiotherapy treatment.

With the advent of multileaf collimators, 3D-conformal radiotherapy technique was able to shape the X-ray beams to match the tumour volume till the advent of radiation beam modulation.

Intensity Modulated radiotherapy(IMRT) is based on the inverse treatment method approach in which the computer is asked to design the optimal approach for achieving the desired dose distribution. Using this approach, higher doses can be concentrated in some parts of the tumor while lower doses can be used in other areas which need protection.

For radiotherapy planning, we now routinely fuse diagnostic imaging with radiotherapy planning images. This fusion enhances our ability to define our target ("Tumour") and even track its motion within the body (4D Radiotherapy). Subsequently using complex computer software and automated algorithms, we can shape the radiotherapy beams to wrap around the tumour and adjust the dose intensity whilst sparing surrounding sensitive organs.

# Rays of Hope in Cancer Care at Kmch - Horizon Scanning

A look at the Past and Future of Radiation Oncology

**Dr. V.S. Kumar, Dr. R. Subramaniam, Dr. R. Madhu Sairam**

Background: Radiotherapy is an important therapeutic tool for treatment of a wide range of cancers and an inseparable component of comprehensive cancer care. It is estimated that about two-third of all cancer patients will receive this as unique treatment or as a part of their complex therapeutic protocol. Radiation therapy can be either with curative or palliative intent and the precise treatment intent will depend on the tumor type,location and stage as well as the general health of the patient.

Radiotherapy is the use of ionising radiation, usually high energy x-rays to treat disease. Radiotherapy is commonly used to treat malignant disease (cancer). It is sometimes used to treat benign tumours and some benign diseases. Radiation treatment is often split into a number of treatments or fractions. These are usually given over a number of days. This allows larger doses of radiation to be given and reduces the amount of normal tissue being treated which can reduce the side effects experienced by patients.

There are 3 main types of radiation treatment

- External beam radiotherapy
- Brachytherapy or sealed source radiation therapy; and
- Systemic radioisotope therapy or unsealed source radiotherapy

Surgery is the most effective way of curing cancer with 49% of all patients cured of cancer being cured by surgery. Some key facts about radiotherapy include:

- After surgery, it is the next most important method of curing cancer.

- 40% of all patients cured of cancer are cured by radiotherapy.
- 50% of all cancer patients will benefit from receiving radiotherapy as part of their cancer management.
- It can offer patients the choice of organ preservation and avoid the need for disfiguring or damaging surgery: For example, instead of mastectomy for breast cancer, breast conservation and radiotherapy can be given. Radiotherapy can also be used for the treatment of certain cancers of internal organs and allow patients to avoid major surgery and retain function, with little or no loss of chance of cure. Examples of this would include cancers of the larynx, prostate and bladder.

## Modern Day High Precision Radiotherapy

In its present form, treatment planning and delivery pathway is sleek, sophisticated and patient friendly. The advent of modern imaging techniques has led to a dramatic improvement in patient experience and treatment outcomes.

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This has been made feasible by the incorporation of various imaging modalities to aid in the planning and delivery of radiotherapy treatment to the target with utmost precision with minimal collateral damage thereby maximising the therapeutic benefit.

The treatment delivery time used to be longer in the past but this has now been reduced with the introduction of Arc therapy (Rapid Arc or VMAT) delivering a precisely-sculpted homogeneous dose distribution with a 360-degree rotation in a single or multi-arc treatment.

In practice, we are able to implement for our patients through the use of "Pre-treatment" imaging such as contrast enhanced computed tomography (CECT) scans, magnetic resonance imaging (MRI), positron emission tomography (PET) scans, and angiography to obtain three-dimensional (3D) structural and biologic information which is used to precisely define the target and thus enable precise and accurate treatment planning

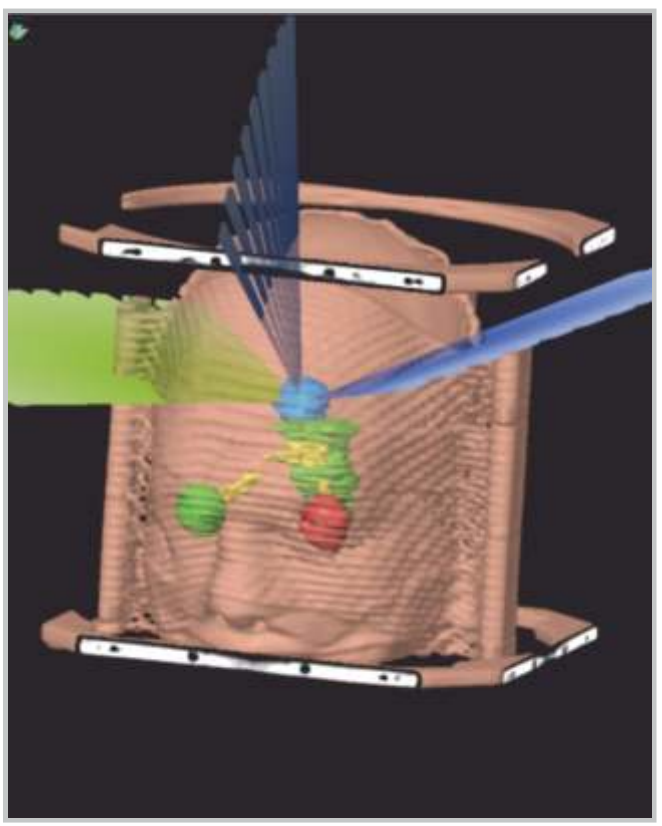
"In-room" imaging methods (Cone beam CT scans, kV X-rays) to obtain periodic information on target position and movement (within the same session or between consecutive sessions), compare it with reference imaging, and give feedback to correct the patient setup and optimize target localization (Image Guided Radiotherapy-IGRT). They also have the potential to provide feedback that may help to adapt subsequent treatment sessions according to tumor response (Adaptive radiotherapy).

From a patient perspective, this has substantially reduced the acute & late toxicity profile thereby improving their Quality of life(QoL) which nowadays is well appreciated. Although there is still a long way to go, radiotherapy treatment is no longer considered a taboo.

Stereotactic Radiosurgery (SRS)

Radiosurgery usually involves treating the target with a single session of radiation treatment (sometimes up to five sessions) with high degree of precision like other modern techniques. This technique was initially used to treat abnormalities within the brain. We are now adopting the same technique to treat other areas outside the brain like lung, liver and adrenal gland (SABR - Sterotactic Abalative Body Radiotherapy).

| | |
|---|---|
| Stereotactic Radiosurgery (Intracranial) | Arterio-venous malformations<br>Acoustic Neuroma<br>Meningioma<br>Brain metastases<br>Cavernoma<br>Trigeminal Neuralgia |
| Stereotactic Ablative body radiotherapy (SABR) | Early Lung cancer<br>Oligometastatic metastatic liver/bone disease<br>Hepatocellular cancer |

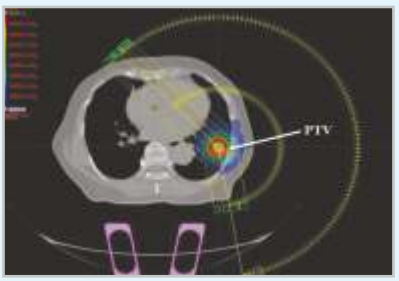


What is Hyperarc? What is the difference between it versus conventional Linear accelerator does.

Traditionally is you see a tumor to target (like the image to the right) , what a conventional linear accelerator will do is target the tumor from one angle and stops rotates and hits it at a different angle . This is referred to as "Step and Shoot".

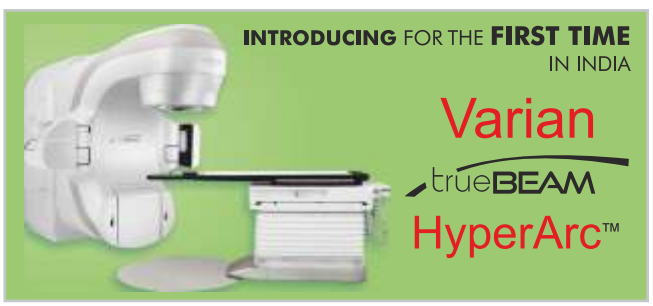
By hitting it from different angles we can minimize the damage to surrounding tissue and focus on the tumor.

What HyperArc does is that it continuously hits the tumor while going through the arc . This is combined with improved collimators (devices used to focus the beam ). Dosimetric studies have shown this to have improved radiation dose delivery to target organ and less to surrounding tissue.




Other benefits are:

- The improved collimators now let it target <4mm such as neural clusters such as in trigeminal neuralgia treatment
- The faster speed with the 4D planning software allow it to highly moving targets like lungs or chest wall
- Improved targeting, faster speed and less radiation to peripheral tissue allows us to treat multiple brain metastasis in one sitting (instead of multiple)




The Future: The progress made in the last decade is fantastic and we foresee the next decade to be even more exciting.

Hypofractionation & Extreme hypofractionation: Whilst improved geographical accuracy has greatly reduced treatment volume this has a provided an opportunity to reduce overall treatment times. So the classical fractionation schedule over 6-7 weeks is being reduced to 3-4 weeks scheme (or even to 3 -5 fractions) is bound to get more prevalent.

Protons & Carbon ions: Expanding our repertoire against cancer and taking advantage of relative biological effectiveness, these two agents has shown promising results for skull base chordomas, chondrosarcomas and childhood tumours. The current limiting factors for this technology are the size and the cost of the machine.

Hyperarc TrueBEAM Technology at KMCH : The Hyperarc Truebeam platform(First of its kind in India) is an innovative, intelligent and intuitive technology which will have the following distinct features.

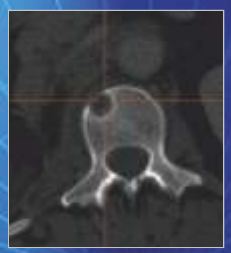
- A completely automated robotic treatment approach with single click treatment delivery
- Much quicker and precise treatment for multiple targets at same time (multiple metastasis in the brain)
- 6DoF Couch which provides utmost precision with sub-millimeter accuracy
- A unflattened Radiation Beam which aids quicker treatment delivery time
- Enhanced Intrafraction Imaging to control patient movement during treatment
- Can treat Neurological diseases as tiny as 4mm diameter (Trigeminal Neuralgia)
- Robust calculation algorithms to provide versatile Treatment Planning Strategy
- Can treat highly moving organs with State of the Art 4D Radiotherapy Facility

Conclusion : The current state of enriched armamentarium has helped cancer patients live longer and as a result the concept of "Life beyond cancer" is starting to be appreciated now and therefore cancer survivorship programmes are being developed to address this issue.

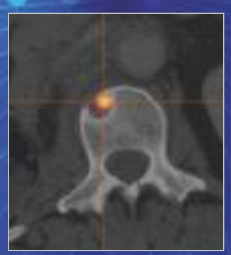
Whilst predicting the future is difficult at best, trends are suggestive of using personalised form of cancer treatment incorporating a wide range of factors-anatomical, physiological, cellular, metabolic and genomic data to help and design patients' cancer treatment.

Radiotherapy treatment will continue to be an indispensable vital tool in our fight against cancer and technological innovations will contribute in changing people's perception and start to recognise cancer as a chronic illness.

## PET Guided Biopsies



NORMAL CT



PET CT

Advantages :

- Using PET to guide procedures allows targeting of lesions that have no cross-sectional imaging correlate, and may also allow targeting of the most viable regions of a tumor.
- Correct target identification results in more confidence by treating physician
- FDG uptake is not affected by procedure

Disadvantages:

- Limitation of PET/CT resolution
- Respiratory or cardiac artifacts may degrade image quality and can cause co-registration errors

## Targeted Radionuclide Therapy of Tumors

Targeted radionuclide therapy is one of the most intensively developing directions of nuclear medicine. Unlike conventional external beam therapy, the targeted radionuclide therapy causes less collateral damage to normal tissues and allows targeted drug delivery to a clinically diagnosed neoplastic malformations, as well as metastasized cells and cellular clusters, thus providing systemic therapy of cancer. The methods of targeted radionuclide therapy are based on the use of molecular carriers of radionuclides with high affinity to antigens on the surface of tumor cells.

# Exploring New Molecular Targets Through 'Theragnostics'

**Dr Ajit S Shinto, Dr K.K. Kamaleshwaran** Department of Nuclear Medicine, KMCH

Our understanding of most diseases especially cancer is evolving at a rapid pace and the game changer has been the identification of specific molecular pathways and changes that are unique to each individual's disease. Thus in oncolcogy now we are able to classify each person's cancer based on the underlying genetic abnormalities, molecular aberrations, receptor expression and presence or absence of certain proteins /peptides etc.

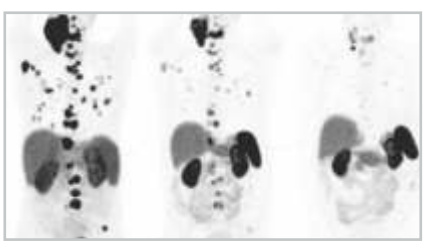
This enables us to tailor the therapy according to each individual disease or personalize medical treatment. Thus we are gradually shifting away from trial and error medicine, where a single type of treatment was used for the same ailment in all patients to precision medicine, where the molecular biology of each individuals disease guides a specific treatment approach.

Nuclear medicine by its virtue of targeting selective molecular pathways is uniquely poised to utilize this individuality for both diagnosis and therapy, especially in cancer. Thus the concept of theragnosis is gaining prominence, where in the same molecule can be used for therapy (Thera) or diagnosis (gnosis). The oldest and most prominent example is the use of radioactive I 131 for both imaging and treatment of thyroid cancer.

The following are a few such new generation molecules ,their diagnostic and therapy images and treatment responses.

### 1.Ga- 68 DOTANOC and Lu-177 DOTANOC as a theragnostic pair.

Here the DOTANOC molecule is a somatostatin receptor (SSTR) analogue which is over expressed in well differentiated neuro endocrine tumors. Below we see the initial diagnostic scan with Ga -68 DOTANOC, which was followed by using serial.



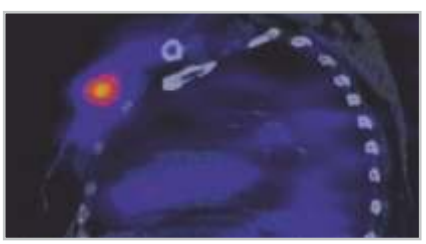
Lu-177 DOTANOC therapies in the same patient for treatment by delivering internal radiation to the tumors cells over- expressing SSTR and then the follow up Ga-68 DOTANOC scans showing good response.

### 2) Ga- 68 PSMA and Lu- 177 PSMA as theragnostic pairs

Prostate specific membrane antigen (PSMA) is an excellent molecular target, which is highly overexpressed in prostate cancer. Below we see a diagnostic Ga-68 PSMA scan in a patient with metastatic castration resistant prostate cancer who was treated with Lu-177 PSMA for selectively targeting cancer cells over expressing PSMA and depositing internal radiation over days with minimal side effects. We see the follow up scan in the last column showing a good metabolic response.

### 3) Lu-177 Trastuzumab

Trastuzumab, an antibody targeting specific receptors is routinely used for treatment of HER 2 positive breast cancers. We have enabled a radioactive labeled trastuzumab, to help the oncologists to see the expression of these receptors inside the patient's body, so that they can see what they are treating and also how the response to treatment is. Below is the image of a patient with excellent localization of the antibody within the chest wall mass in a case of metastatic ca breast with HER 2neu positivity.



**Conclusion** : We are further working on extending its use to do therapeutic interventions where in we could have a double effect, both of the antibody itself and then the selective internal radiation too, So that the treatment effect is in fact amplified. Serial scans could also be used for treatment response assessments as well.

Our department features some of the most advanced research and cutting edge clinical applications, some of which are done for the first time not only within the country but also some times world wide.

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# Intraperitoneal Chemotherapy - Treatment Unexplored ??

**Dr. Firoz Rajan** MS., MCh (Surgical Oncology)., Consultant Surgical Oncologist

For EPIC: Our analyzed results of 41 patients who had undergone the procedure show a median PFS of 28 months when studies from all over the world report a PFS of slightly over 12 months with standard therapy of surgery and chemotherapy.

*Dr. Firoz Rajan*

Introduction : Described initially in the 1950s for treatment of malignant ascitis , IP chemo is rarely used in treatment of cancer. Exemplary studies on the pharmacokinetics of drug diffusion across the peritoneal surfaces by Dedrik in the 70s proved that a theoretical advantage existed in the use of chemotherapeutic drugs when used intraperitoneally due to the peritoneal – plasma barrier. This results in a tumor on the peritoneal surfaces being exposed to a higher concentration of drug than that could be achieved intravenously. Recent interest in this approach with addition of heat by Heated Intraperitoneal chemotherapy (HIPEC) has expanded the scope of surgery in approaching these conditions of Peritoneal Carcinomatosis (PC) with a curative intent rather than treatment with palliative chemotherapy.

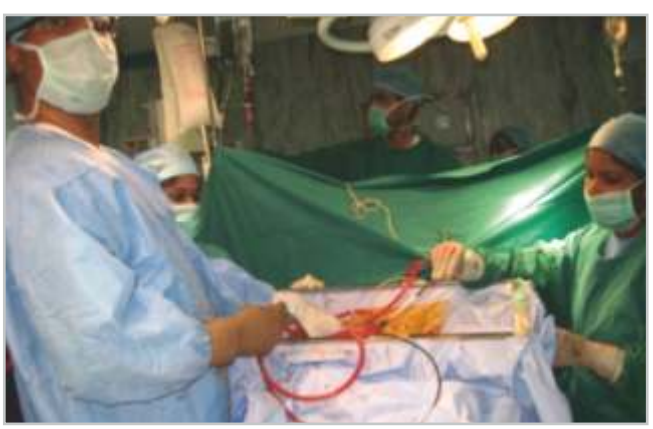
Incidence of PC : The true incidence of PC is unclear because of the heterogeneity of published methods and findings. PC develops in 4% to 19% of patients after curative surgery, in up to 44% of patients with recurrent colorectal cancer, and in 40% to 80% of patients who die from disease. Certain other cancers like Ovarian cancers present with disease dissemination in more than 75 % of cases. Then there are the cancers like Appendiceal cancers ,pseudomyxoma peritonii (PMP) and mesotheliomas where intravenous chemotherapy hardly makes any effect .

Pharmakokinetics : The basic principle by which IP chemo acts is by drug diffusion. So there is a critical size (2-2.5 mm ) of the tumour nodules below which the IP chemo is going to be effective . Also the molecular weight and the hydrophilic nature of the drug are also important . Area Under Curve (AUC) indicates the extent to which the IP chemo is going to be effective considering the clearances of the drug from peritoneum and plasma. The commonly used drugs for IP chemo are Cisplatin ( AUC 20 :1) , Mitomycin ( 24 :1) , 5 FU ( 250 :1) , Paclitaxel (1000 :1) . Needless to say that such concentrations cannot be achieved if they are given intravenously (as the toxicity will be incompatible with life) , therefore completely overcoming the issue of drug resistance.

Methods of IP chemotherapy : The following are the commonly used methods of IP chemo

- Heated Intraperitoneal chemotherapy (HIPEC) and Bidirectional Chemotherapy (IV chemo + HIPEC) – performed in the operation theatre after cytoreductive surgery.
- Early post op IP chemotherapy (EPIC) - performed in ward with drain or catheter
- Sequential IP chemotherapy - performed with a port or catheter and over a period of time
- Neoadjuvant IP chemotherapy - for gastric & ovarian cancers.

HIPEC : Has been popularized by Dr Sugarbaker in the 1990s for the treatment of Appendiceal cancers and Pseudomyxomas . The Peritoneal Carcinomatosis Index (PCI) and its corollary CT – PCI (after imaging) scoring system described is universally accepted to prognosticate and predict the success of treatment. A number of cytoreductive surgeries ( peritonectomies and visceral resections) described which help to remove all visible disease from the peritoneal surfaces is performed followed by the recycling of heated (41-42 C) chemotherapy fluid in the peritoneal cavity for a period of 90 minutes . Heat potentiates the effect of chemotherapy and improves diffusion of drug into the residual



tumour nodules. A dedicated hyperthermia pump machine is used for recycling the drug . The completeness of cytoreduction score (CC score) helps to objectively assess the extent of residual disease after CRS and only patients who have a CC score of 0 / 1 (Upto 2.5 mm) are subject to the HIPEC procedure. This intraoperative heated chemobath procedure ensures that the entire peritoneal surfaces are exposed to the drug.

EPIC : Administer the IP therapy immediately after surgery is referred to as early postoperative IP chemotherapy (EPIC). EPIC is usually done as multiple consecutive daily doses of IP therapy are instilled into the peritoneal cavity before the adhesions set in the peritoneal cavity. Several retrospective studies indicate a higher morbidity when HIPEC is combined with EPIC than with HIPEC alone. It has been described for colorectal , appendiceal , PMP and ovarian cancers.

Results : With the rapid acceptance of the procedure of HIPEC and improved training programmes for cytoreductive surgery , the number of centres which have embraced this procedure increased exponentially in the last decade or so . A number of randomized trials have shown the Progression free survival (PFS) and overall survival (OS) benefit of the procedure in ovarian cancer in the primary, interval and recurrent settings. Currently there is a lot of interest for this treatment as the biology of Ovarian cancer where the disease usually recurs in the peritoneal cavity is conducive for this type of therapy. International trials support the use of IP chemotherapy in the management of ovarian cancer with peritoneal dissemination.

- When it comes to the management of Appendiceal neoplasms and PMP, HIPEC has shown unmatched results with 2/3 of them surviving 10 years with some survivors reaching 20 years !! Results previously unheard of .
- HIPEC has been used for Peritoneal Carcinomatosis of colorectal origin with retrospective studies showing a median overall survival of 4 years ! But a recent randomized trial with Oxaliplatin as the IP chemo agent in HIPEC did not show the advantage in the HIPEC arm .
- Peritoneal Mesotheliomas which present with resistant ascitis has a durable treatment response with HIPEC with more than 80 % showing long term control of ascitis .
- Morbidity rates can reach 50 % with usual morbidity being neutropenia, sepsis, leaks , abdominal collections . Mortality rates are compatible to any major intraabdominal surgery and steadily declines with experience.

**KMCH Experience**

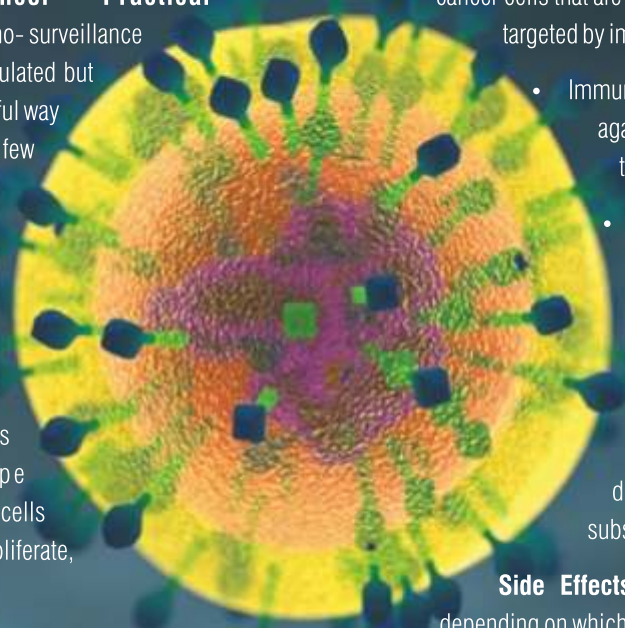
HIPEC: KMCH is the only centre in western Tamil Nadu which has an established HIPEC programme with more than half a dozen procedures performed. Initially it was done for Ovarian cancers, but presently it is preferred method of treatment for Appendiceal and pseudomyxomas and rarely occurring mesotheliomas. The cost of treatment is kept low with the apt use of the cardiac bypass machine instead of the costly 'dedicated hyperthermia machine' .

EPIC: IP chemo in the form of EPIC is routinely offered to patients of advanced cancer ovary in addition to standard chemotherapy with a good number of patients showing prolonged cancer progression free survival unheard of in this disease condition. EPIC as followed by western methodology can be quite costly . KMCH uses a modified EPIC regimen which brings the cost down considerably.

The results of this modified EPIC regimen is very promising . Morbidity was more or less manageable with this treatment the majority being prolonged ileus and neutropenia. Our analyzed results of 41 patients who had undergone the procedure show a median PFS of 28 months when studies from all over the world report a PFS of slightly over 12 months with standard therapy of surgery and chemotherapy.

# Brief Overview of Immunotherapy

**Dr. Bharat Rangarajan** MD.,DM.,ECMO., Consultant Medical Oncologist



**Immunotherapy in Cancer - Practical Applications in 2019** Immuno- surveillance in cancer has been long postulated but has never been a very successful way of treating cancer barring a few example until recently.

The T cells in the circulation can recognize Tumor associated antigens/ neo-antigens and mount an immune response against the cancer. However cancer cells develop many " escape mechanisms" from these T cells and continue to survive, proliferate, and metastasize

Using the body's Immunity to fight cancer: The 2018 Nobel Prize in Physiology or Medicine was awarded to James P. Allison and Tasuku Honjo "for their contribution to cancer therapy by inhibition of negative immune regulation". Their pioneering work on the CTLA4 and PD1 immune checkpoints revealed that these pathways act as so-called 'brakes' on the immune system, and showed that inhibition of these checkpoint pathways allows T cells to more effectively eradicate cancer cells.

The PD L1 on tumor cells and PD 1 on T cell binding causes a BRAKE on the immune systems. Similarly the CTLA 4 on T cells can inhibit the co-stimuatory molecules and apply a BRAKE on the Immune system mediated cancer cell killing.

CTLA 4 Inhibitors, PD 1 Inhibitors and PD L 1 inhibitors RELEASE THE BRAKE on the immune systems and allows our Body's Immunity to attack the cancer cell.

**Advantages** :

- Activated and tumor-specific immune cells can reach areas that a surgeon cannot, and target even microscopic disease and disseminated metastases.
- Immunotherapy does not preferentially attack dividing tumor cells, as chemotherapy and radiation therapy usually do. Thus, cancer cells that are slowly dividing might be more efficiently targeted by immunotherapy.
- Immunotherapy might strike more specifically against the tumor, thus lowering the damage to surrounding healthy tissue.
- Memory cells can suppress the re-emergence of the cancer. Long-term control or even complete eradication of the disease is possibly the biggest promise that immunotherapy holds for the future, as induced anti-tumor responses have sometimes proven durable over many years, at least in a subset of patient

**Side Effects** of cancer immunotherapy will vary depending on which type of immunotherapy is used. They are usually related to stimulation of the immune system and can range from minor symptoms of inflammation (e.g., fever) to major conditions similar to autoimmune disorders.

**KMCH Case Experience** Ms. NV , 58 year old Home maker presented with Fracture of left humerus. The X ray was suggestive of Pathologic fracture and further evalautaion revealed Lung Mass with multiple bone metastsis (Figure 3 - PET CT). The biopsy was Moderately differentiated Adenocarcinoma with no Targetable / Actionable mutation (EGFR No activation mutation, ALK, ROS 1 and Her 2 neu Negative) and PD L 1 expression on tumor by IHC was99%.

She was started on Immunotherapy with Pembrolizumab and had Near CR on PET after 3 cycles with significant clinical improvement(Figure4 – PET CT )

**Conclusion:** Immunotherapy is the exciting new therapeutic strategy to fight cancer by stimulating the body's defense mechanisms/ T cells and will revlotionize cancer care in the coming decade. The Medical Oncology department at KMCH offers Immunotherapy for appropriate patients and is committed to delivering the best and recent treatment options your patients.

# Targeted Therapy in Brief

**Dr. Vignesh Kanda Kumar B** MD.,DM., Consultant Medical Oncologist

### What is Targeted Therapy ?

Targeted therapy works by targeting specific genes, proteins or the tissue environment that contributes to cancer cell growth and survival. These genes and proteins are found in cancer cells or in cells related to cancer growth like blood vessel cells. Medication target these specific genes and proteins and thereby

Researchers are learning that specific gene changes take place in certain cancers. So they are developing drugs that target the changes. The drugs can:

- Block or turn off signals that tell cancer cells to grow and divide
- Keep cells from living longer than normal – Destroy the cancer cells

### Types of Targeted Therapy

Monoclonal Antibodies: Drugs called "monoclonal antibodies" block a specific target on the outside of cancer cells and/or the target might be in the area around the cancer. These drugs work like a plastic cover you put in an electric socket. The plug keeps electricity from flowing out of the socket. Drugs called "monoclonal antibodies" block a specific target on the outside of cancer cells and/or the target might be in the area around the cancer. Monoclonal antibodies can also send toxic substances directly to cancer cells. For example, they can help chemotherapy and radiation therapy get to cancer cells better.

Small-Molecule Drugs: Drugs called "small-molecule drugs" can block the process that helps cancer cells multiply and spread. Angiogenesis inhibitors are an example of this type of targeted therapy.

*Below are a few examples of targeted therapies*

Breast Cancer: About 20% to 25% of all breast cancers have too much of a protein called human epidermal growth factor receptor 2 . This protein makes tumor cells grow. If the cancer is HER2 positive, several targeted therapies are available

Colorectal Cancer: Colorectal cancers often make too much of a protein called epidermal growth factor receptor (EGFR). Drugs that block EGFR may help stop or slow cancer growth. These cancers have no mutation in the KRAS gene. Another option is a drug that blocks vascular endothelial growth factor This protein helps make new blood vessels

Lung Cancer: Drugs that block the protein called EGFR may stop or slow lung cancer growth. This may be more likely if the EGFR has certain mutations. Drugs are also available for lung cancer with mutations in the ALK and ROS genes. Doctors can also use angiogenesis inhibitors for certain lung cancers.

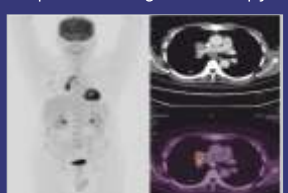
Melanoma: About half of melanomas have a mutation in the BRAF gene. The FDA has approved several BRAF inhibitors. These drugs can be dangerous if you do not have the BRAF mutation.

### Advantages of targeted therapy include:

- Potentially less harm to normal cells,
- Fewer side effects,
- Oral formulations are easy to administer, better compliance with good quality of life.

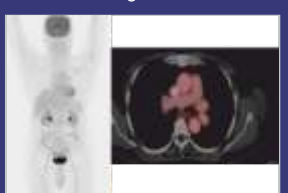
Medical oncology as a science is fast evolving with more and more precise targeted treatments. Results to targeted treatments are promising and are far better than what it was a decade back. There are multiple case reports of Stage 4 metastatic cancers such as adenocarcinoma of the lung which have gone into disease regression and are in remission for greater than 2 years

Case Report: 55 year old gentleman with clean habits presented with dry cough and vague right chest pain of 2 months duration. He on examination had right supra clavicular node. Biopsy of supra clavicular node was suggestive of adeno carcinoma. PET CT scan showed right hilar mass with bilateral lung nodules and pleural effusion. He was diagnosed to have stage IV adeno carcinoma lung after immuno histochemistry confirmation. Paraffin blocks of his node biopsy was sent for genomic alteration studies. He had ALK (anaplastic lymphoma kinase) re arrangement. He was started on palliative tablet. crizotinib 250mg twice daily. Within 2 weeks his cough and chest pain settled. He was continued on tablet crizotinib with tolerable side effects. PET CT scan done after 6 months of tablet. Crizotinib showed excellent response to targeted therapy. Presently he has completed 10 months of targeted therapy and he is continued on the same drug.



Pretreatment PET scan
FDG uptake at multiple metastatic sites

Post treatment PET scan
No longer has FDG uptake



# HRT in Gynecologic Cancers
# Is Our fear leaving Women Behind ?

**Dr Anbukkani Subbian** DGO.,DNB.,MRCOG(UK).,Fellow in Gyn. Oncology.,
Consultant Gyn. Oncology

Introduction: About 30-40% of gynecologic cancers occur in pre and perimenopausal women. The impact of removal of uterus and the ovaries and the abrupt surgical menopause that ensues has a huge physical and emotional impact on these women. With better survival outcomes being attributed to medical advancement, addressing the effects of surgical menopause becomes an important part of giving these women better quality of life. In reality, however, most oncologists hesitate to prescribe hormone replacement therapy, even when strongly indicated, due to the fear of possibly triggering a recurrence or adversely affecting survival outcomes. Adding fuel to fire, is the fallout of the World Health Initiative and Million Women study which shook the basis of HRT which was being prescribed for bone and cardio-protection in women not affected by cancer. So then, in women with genital tract cancers, are these fears justified or unfounded? This article aims to look into current scientific evidence to suggest practice guidelines for prescribing HRT/alternatives in women affected by genital tract cancers.

Endometrial cancer is the most common gynecological cancer in many parts of the world. About 80% of endometrial cancers diagnosed are the estrogen dependent endometrioid type. The treatment of endometrial cancer includes removal of ovaries because of risk of metastasis, coexistent ovarian cancer and because estrogen from ovaries may increase the risk of recurrence. This estrogen relatedness is the prime reason for the hesitation in prescribing HRT to women with endometrial cancers requiring treatment of menopausal symptoms. It also brings up suggestions that estrogen in these women should be prescribed along with progesterone to negate its stimulatory effect. Existing evidence, however, suggests that this fear may be theoretical. Recent metaanalysis by Shim et al showed that there was no significant increase in the risk of recurrence in HRT users following endometrial cancer versus controls. The number of recurrences was 19 among the 896 HRT, whereas there were to 64 recurrences in 1079 controls.

The only RCT in this area was conducted by the Gynecologic Oncology Group. 618 patients with stage I–II endometrial cancer treated with estrogen after surgery were compared with 618 matched placebo controls. After a median follow-up of 35.7 months, the recurrence rates were 2.3% and 1.9% in the treatment group and controls, respectively. The conclusion was that the relative risk of recurrence and death from estrogen therapy after treatment for early stage endometrial cancer was 1.27 but this was not significant and the risk of recurrence was exceedingly low.

Based on level I-III evidence, it would be reasonable to say that Estrogen Replacement therapy(ERT) can be prescribed in small doses for a short duration to low risk, early stage endometrial cancers as the risk of recurrence is low, with or without HRT. The objective would be to improve quality of life if menopausal symptoms were troublesome.

Ovarian Cancer: Approximately 60 – 70% of ovarian cancers are diagnosed in stage III/IV and only 30% of these women will be alive after 5 years. The issue of menopause management is still important as 40% of these tumours will occur in women between 30 – 60 years of age.

The theory of estrogen stimulation resulting in ovarian carcinogenesis has very little supporting clinical data. Although in vitro and some in vivo studies show that ovarian cancer cell growth may be accelerated by estrogen, this has not been replicated in clinical studies.

Recent meta-analysis which included two RCTs and four observational studies, suggested that HRT use after surgery for ovarian cancer had a favourable impact on OS (HR =0.69), but when these studies were categorized into cohort study and RCT subgroups, not all of them demonstrated positive results. The meta-analysis of cancer recurrence of three available studies demonstrated that postoperative HRT use was not associated with an increased risk of recurrence in ovarian cancer survivors and this pattern also emerged in the subgroup analysis for the stage and type of HRT. Data regarding the type of HRT, duration of use and effect of HRT on tumours expressing Estrogen receptors is unknown due to lack of data.

In effect, symptomatic women may be prescribed HRT postoperatively only after counselling about the level of evidence currently available.

Cervical Cancer: Although cervical tissue expresses estrogen receptors, most squamous carcinomas and adenocarcinomas of the cervix are not hormone dependent. Ovaries can be preserved in squamous carcinomas, but are usually removed in adenocarcinomas due to slightly higher risk of metastasis. There are no randomised trials on the use of HRT in women with cervical cancers treated with surgery or radiation therapy. Prospective cohort studies show that use of HRT in cervical cancer do not worsen survivals. Hence it may be considered in this scenario on a per case basis( Level II-III)

Alternative Therapies: Alternative therapies for treatment of various menopausal symptoms are well known. The most established of these are selective serotonin reuptake inhibitors for management of hot flushes. Although, there are no studies of their use in gynecologic cancers, they may be considered as a reasonable alternative. It would be reasonable to say that the current recommendation of using the smallest dose of HRT for the shortest length of time required will be applicable to cancer survivors as much as it applies to other women. The evidence exists in endometrial cancers which is considered the most hormone dependent cancer among gynecologic cancers. In the other cancer groups it should be individualized.

# Evidence Based Medicines Vs The Alternatives

**Dr R. Madhu Sairam** Department of Radiation Oncology

A new observational study published by JAMA in 2018* strongly concludes that people who choose alternative therapy as the exclusive initial treatment tend to have poorer survival. (* - JAMA Oncol. 2018;4(10):1375-1381.) In this cohort study of 1,901,815 patients, use of complementary medicine varied by several factors and was associated with refusal of conventional cancer treatment, and with a 2-fold greater risk of death compared with patients who had no complementary medicine use.

*Dr. R. Madhu Sairam MBBS.,MD (RT)., Consultant Radiation Oncologist*

Introduction: As practitioners of allopathic system of medicine, supposedly the 'mainstream' medical treatment and as men of science whose training comes from a long-drawn medical curriculum, we shut our eyes to other existing medical systems. 'Alternative medicines' have penetrated every facet of health care system and are no longer restricted to a few individuals. It is a world-wide phenomenon. It's an undeniable fact that alternative medicines have made unprecedented inroads into oncological management in our country as well. Let's take a critical look at this major public hazard.

Alternative medicines like Ayurveda, herbal remedies have existed for centuries and have been passed on over generations to this date. But why should they pose a hazard now? Such therapies are not entirely backed by evidence or proven to cure major medical illnesses especially 'Cancer'. Nevertheless, even western countries seem to be battling 'Chinese remedies' and Tibetan herbs etc. Alternative medicine is not wholly restricted to ingestible forms but features some acupuncture, touch therapy, Qi gong and the likes.

### Why do people chose 'alternative' over mainstream?

The social preconception among Indians that surgery, radiotherapy and chemotherapy offered as cure for cancers may be extremely toxic and intolerable to their kin. For fear of side effects most families simply choose easier options sometimes fully well knowing that likelihood of cure is remote. Most oncologists fail to convince patients and relatives that side effects have to be endured for better good.

Most families consider oncology medicine as impersonal and feel there lacks a potential gap between patient expectations and doctor's choice.

We must also admit that consultation time may be inversely proportional to the popularity of the therapist. People are known to wait endless hours to collect special barks and herbs from renowned ashrams and babas. Such scientific illiterates don't seem to mind the absence of 'personal treatment' and end up collecting same bark for all disease ranging from thyroid cancers to glioblastomas. I must admit that my childhood friend travels to a remote place in northern hills of western ghats every month to collect medicines for his mother diagnosed with Follicular adenoma and refused surgery for fear of losing voice. I have given up rationalizing with the family and now I enjoy a share of fresh forest honey after every arduous trip to the ashram.

Drugs and medicines which carry 'natural and organic' tags are perceived as non-toxic and body-friendly whereas most 'kashayams and arishtams' carry toxic heavy metals.

I remember seeing a patient with early operable tongue cancer who opted for alternative medicines. 6 months after consuming the medicines developed ascending motor weakness which was diagnosed to be lead (Pb) toxicity. Not only did his cancer progress to become incurable but his general condition worsened drastically.

While doctors battle the effects of google doctor, we find people being lured by spurious websites claiming complete cure for cancers with simple herbs. Going one step further, many herbal medical practitioners have a large following on microblogging sites, run paid facebook pages, promote shamelessly through several social platforms and go on to keep tight hold on customers through WhatsApp groups.

### Implications for alternative therapies

Perhaps of greater importance is the implications of aberrant and unscrupulous use of unproven therapies in individual patient outcomes which translates into poor survival stats across the nation. The observational study published by JAMA strongly concludes that people who choose alternative therapy as the exclusive initial treatment tend to have poorer survival.

Patients and their families spend months on end with unrealistic hopes of cure whereas the cancer might progress unabated. Many tend to ignore fungating masses and worsening symptoms as possible signs of recovery. It's appalling to notice that choosers of alternative medicine don't even carry the guilt of making wrong choices once they find that cancer has advanced beyond cure.

It's hard not to mention the prevailing social myths pertaining to cancer management which fuels irrational use of alternative medicines. Many people freak out with the very idea of performing biopsies for cancer diagnosis. Most vaidhyars don't insist on getting a biopsy ( understandable; its a worthless exercise when the treatment is all the same!) Or even insist on seeing the patients. At times, a mere 'katti' in any part of the body would suffice to procure a concoction of herbs that come with peculiar caveats like abstinence from milk, egg, curd and all white coloured edibles or restriction on non-vegetarian diet. A sizeable number succumb to imposed malnourishment.

I have encountered an argumentative Indian in practisc who'd go any length to defend Ayurveda medicines that he was consuming along with chemotherapy for a metastatic disease. His unflinching faith comes from the fact that his insightful neighbor found cure with herbs for a long standing neck lump which he even refused to biopsy. On the advise of a general medical practitioner started on empirical anti-tuberculous therapy to which he developed complete response of all nodes. All his acquaintances believe its the magic herb that cured his cancer!

Sparing a few ashrams and gurukulams most alternative therapists fleece their customers. Costs of therapy plummets in direct proportion to the anxiety of the by-standers. Some families on whom enlightenment dawns after months of failed trial of herbal medicines stand penniless after exhausting resources on worthless drugs.

### Unperceived Benefits of Modern Medicine

Oncological therapies have undergone transformations for the better in the last two decades. Tremendous achievements have been made in terms of achieving cure for certain cancers and reducing collateral damage. Patients can certainly continue to have excellent quality of life following multimodality therapy. Surgeries have become less aggressive, radiation schedules shortened and sophisticated and chemotherapy more personalised than earlier. So it's the responsibility of treating doctor's to convince patients to undergo treatments and also on the society as a whole to understand consequences of appropriate therapy and keep faith in modern medicine and not in miracles.

To check on shady unschooled healers and bring strict regulations on who should prescribe and practise is the solemn responsibility of the government. As responsible citizens and contributors to people's wellbeing, practitioners of modern medicine can only influence people who trust in them and educate those who are willing to listen.

## Awards

*Dr Jenny Gandhi*
*Best IR Fellow*

*Dr Elango S*
*Best Scientific Paper ISVIR*

*Dr Rinoy R Anand*
*1st Place in National Level Quiz*

# Complementary Medicine, Refusal of Conventional Cancer Therapy and Survival Among Patients With Curable Cancers

**Skyler B Johnson** MD1; **Henry S Park** MD, MPH1; **Cary P Gross** MD2; **et al James B Yu** MD, MHS1,2

Author Affiliations : JAMA Oncol. 2018;4(10):1375-1381. doi:10.1001/jamaoncol.2018.2487

Abstract Importance: There is limited information on the association among complementary medicine (CM), adherence to conventional cancer treatment (CCT), and overall survival of patients with cancer who receive CM compared with those who do not receive CM.

Objectives: To compare overall survival between patients with cancer receiving CCT with or without CM and to compare adherence to treatment and characteristics of patients receiving CCT with or without CM.

Design, Setting and Participants: This retrospective observational study used data from the National Cancer Database on 1 901 815 patients from 1500 Commission on Cancer–accredited centers across the United States who were diagnosed with nonmetastatic breast, prostate, lung, or colorectal cancer between January 1, 2004, and December 31, 2013. Patients were matched on age, clinical group stage, Charlson-Deyo comorbidity score, insurance type, race/ethnicity, year of diagnosis, and cancer type. Statistical analysis was conducted from November 8, 2017, to April 9, 2018.

Exposures: Use of CM was defined as "Other-Unproven: Cancer treatments administered by nonmedical personnel" in addition to at least 1 CCT modality, defined as surgery, radiotherapy, chemotherapy, and/or hormone therapy.

Main Outcomes and Measures : Overall survival, adherence to treatment, and patient characteristics.

Results: The entire cohort comprised 1 901 815 patients with cancer (258 patients in the CM group and 1 901 557 patients in the control group). In the main analyses following matching, 258 patients (199 women and 59 men; mean age, 56 years [interquartile range, 48-64 years]) were in the CM group, and 1032 patients (798 women and 234 men; mean age, 56 years [interquartile range, 48-64 years]) were in the control group. Patients who chose CM did not have a longer delay to initiation of CCT but had higher refusal rates of surgery (7.0% [18 of 258] vs 0.1% [1 of 1031]; P < .001), chemotherapy (34.1% [88 of 258] vs 3.2% [33 of 1032]; P < .001), radiotherapy (53.0% [106 of 200] vs 2.3% [16 of 711]; P < .001), and hormone therapy (33.7% [87 of 258] vs 2.8% [29 of 1032]; P < .001). Use of CM was associated with poorer 5-year overall survival compared with no CM (82.2% [95% CI, 76.0%-87.0%] vs 86.6% [95% CI, 84.0%-88.9%]; P = .001) and was independently associated with greater risk of death (hazard ratio, 2.08; 95% CI, 1.50-2.90) in a multivariate model that did not include treatment delay or refusal. However, there was no significant association between CM and survival once treatment delay or refusal was included in the model (hazard ratio, 1.39; 95% CI, 0.83-2.33).

Congratulation

**Dr Kannan G**

*Consultant Radiologist, Department of Radio Diagnosis*

has cleared the prestigious European diploma in radiology (EDiR) held in Vienna Feb 2019

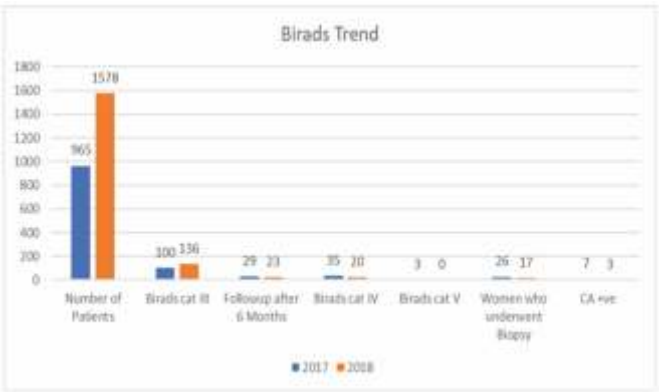
# Women's Health Corner - Our Communication Failure in Breast Cancer

**Dr Smitha Ashok** MBBS.,DNB.,DFM.,D.DIAB., Consultant Physician

*Dr. Smitha Ashok*

In an Screening Mammography Audit , Out of the 1000 plus number of women in the year 2017 , and 1500 plus women in the year 2018 who subjected themselves for USG breast / mammogram the following outcome is tabulated under.

Excluding the normal findings and non cancerous findings, the result obtained is as follows.




Breast Image Reporting And Data System (BIRADS)

1. Negative mammogram [BIRADS1]
2. Benign finding[BIRADS2}
3. Probably benign[BIRADS3]
4. Suspicious abnormality[BIRADS4]
5. Highly suggestive of malignancy[BIRADS5]
6. Known biopsy proven malignancy[BIRAD6]

BIRADS category III patients are advised a mandatory follow up after 6 months to reassess the condition . BIRADS category IV and V are advised biopsy at the earliest.

Of all the 30 women who underwent core biopsy in 2017, 7 women were confirmed with definitive cancer. Of the 16 women who underwent biopsy in 2018, 3 women were confirmed positive for cancer. Rest of the patients were found to have Fibroadenomatous or fibrocystic changes. Needless to mention, they all were totally asymptomatic at the time of presentation for annual MHC, and it was their routine checkup which helped them clinch with the earliest diagnosis.

Common challenges faced in the Hospital.

- Despite detailed explanation and positive assurance, only 20 to 30 % of women belonging to BIRADS category III reported for a follow up after 6 months.
- 15 to 25 % of women who have been diagnosed with suspicious lesion (BIRADS category IV and BIRADS category V) were still hesitant to subject themselves for biopsy / MRI study, fearing for any negative outcome.
- There were cases where even biopsy proven carcinoma patient did not come for further surgical treatment or chemotherapy, despite intensive counseling to patient and her relatives.

In the department of MHC, where most of the screening mammograms are done , we strive to create an awareness to the patients that early detection of breast cancer ensures 100% curable rates and the chances of survival is the highest in them. We also reiterate that patients need not fear complete removal of breast if detected early. We convey that breast conservation surgery in the form of lumpectomy and removal of some breast tissue around, will suffice in such patients.

Patients are referred to the KMCH Breast Center in our hospital headed by Dr. Rupa Renganath. To try to improve outcomes and allay fears ,a separate department outside of normal radiology – 'a safe space ' was created . Special counselling area was created.

Triple assessment method (clinical examination, imaging, possible biopsy) is done within a short span of time, under one roof.

KMCH has equipped the center with

- Fully automated state of the art digital mammogram with tomosynthesis
- Dedicated 'Supersonic' Ultrasound to differentiate breast tissue
- Dedicated Team to track patients and counsel them
- Vaccutome - Suction biopsy device

Further auditing will reveal whether these changes have improved outcomes.

However, large scale communication is needed to spread the message that Breast cancer is curable. Otherwise we failed before we began

# A Rare Large Cystic Tumour of Pancreas - Case Report and Literature Review

**Dr. Maheswaran Pitchaimuthu, Dr. Paari Vijayaragavan, Dr. Selvakumar, Dr. Arulraj Ramakrishnan, Dr. Aravindhan**
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Introduction: Pancreatic neuroendocrine tumors (PanNETs) are typically solid neoplasms but in rare instances may present as cystic lesions. This unusual presentation can make clinical diagnosis challenging. In addition, the clinical and histopathologic characteristics of cystic PanNETs are poorly defined. Similar to solid PanNETs, cystic PanNETs develop with an equal sex distribution and over a wide age range (23 to 91 y; mean, 52 y). The unusual cystic appearance make radiologic differentiation from other cystic pancreatic neoplasms difficult with a misdiagnosis. Here with we present a case of successfuly treated large cystic neuroendocrine tumour of the pancreas.

Case Report: 62 years old pleasant lady presented to us with colicky abdominal pain over a period of 2 months. She has no significant past medical history apart from peuperal sterilisation. She consulted a GP outside and was treated as dyspepsia. Since her symptoms did not improve after few weeks she consulted another doctor, who organised an ultrasound scan. The ultrasound scan showed a large cystic lesion in the abdomen, probably arising from the pancreas. Because of this finding – she was referred to us.

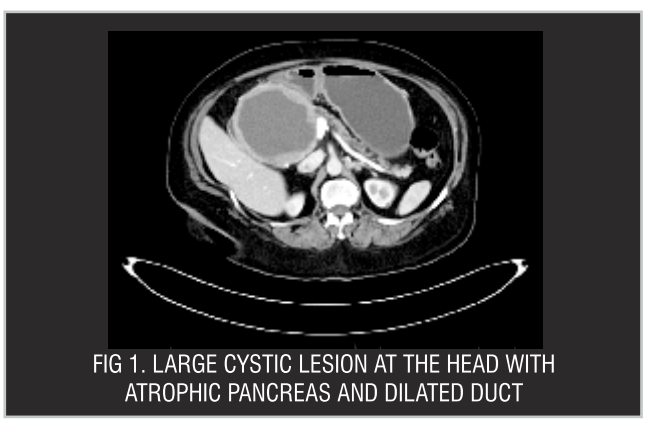

FIG 1. LARGE CYSTIC LESION AT THE HEAD WITH ATROPHIC PANCREAS AND DILATED DUCT

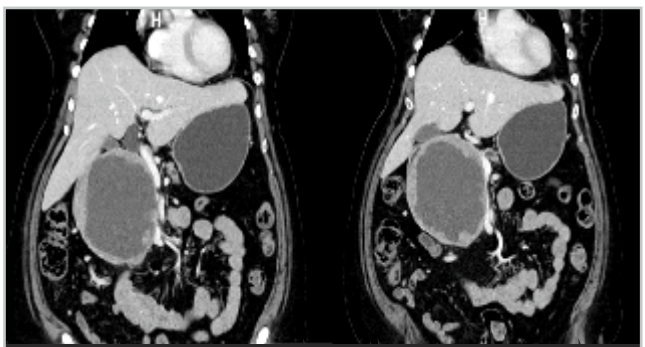

FIG 2: LARGE CYSTIC LESION OF PANCREAS COMPRESSING PORTAL AND SUPERIOR MESENTERIC VEIN

On clinical examination, she was obese with stable vitals. There was no pallor, jaundice, generalised lymphadenopathy. Abdominal examination showed palpable mass in the right hypochondrium. We organised a CT scan of chest, abdomen and pelvis.

CT scan of the abdomen showed - There is well-defined hypodense lesion with irregular enhancing wall (upto 1.3 cm thick) is seen in the head and uncinate process of the pancreas, measuring 10 x 10.3 x 12 cm (Figure 1). No calcification / enhancing septa / scar. In the medial aspect the lesion causes significant narrowing of portal vein/SMV (approximately 9cm) with loss of fat plane (Figure 2). SMA is seen separately. The lesion causing mass effect over the proximal CBD causing upstream dilation of CBD (diameter 1.5 cm) and central intrahepatic biliary radicals. CT chest - did not reveal any distant metastases. All her labs including CA19-9 levels, were with in normal limits. With the provisional diagnosis of mucinous cystic neoplasm - she was counselled for whipple's procedure. Patient and family were explained about the procedure and informed consent obtained.

Procedure: She had initial laparoscopy - to rule out peritoneal

disease. Then her abdomen was opened with roof top incision. Intraoperative findings as follows:

- Large cystic lesion arising from the head of the pancreas compressing PV and SMV
- Large branch from SMV supplying the lesion - required resection and suturing the defect in SMV
- Mesocolon adherent to the cystic lesion - middle colic vessels ligated
- Thin walled gall bladder with multiple stones and dilated CBD
- Firm pancreas with dilated MPD (4-5mm)
- Few hepato-dudoenal lymphnodes.
- Paraumbilical hernia - omentum as a content
- No evidence of liver/peritoneal metastases or free fluid in the abdomen

Patient underwent successful pylorus preserving pancreatico duodenectomy (PPPD). Even though the portal vein and SMV were adherent to the tumour, they were released completely without any oncological compromise (Figure 3) and the whole tumour was removed (Figure 4). Standard reconstruction was performed.

Histology: Pathological examination shows a tumor in the head of pancreas. The tumor is encapsulated with a thick capsule and focal capsular dehiscence involved by tumor. The tumor is composed of sheets, trabeculae and acinar pattern of arrangement with delicate rich vascular network. The cells are relatively uniform and show finely granular amphophilic to eosinophilic cytoplasm, centrally located round to oval coarsely clumped nucleus with distinct nucleolus. Mitosis upto 3/2 mm2 is seen. Tumor necrosis, haemorrhagic areas are seen and central areas show cystic degeneration with cystic and hemosiderin laden macrophages. All margins clear of tumour. 21 lymphnodes found and were free of tumor.

Post OP Course: Her postoperative period was uneventful and she was succesfully discharged on Day 6. Her case was discussed in tumour board and decided for adjuvant therapy. Since she preferred to have chemotherapy close to her place, she was discharged and advised to see medical oncologist locally. On 5 months follow up – she is doing well with no evidence of recurrence (had PET -CT done outside).

Discussion: Pancreatic neuroendocrine tumors (PanNETs) are rare neoplasms that comprise up to 5% of pancreatic malignancies. These neoplasms have an estimated incidence of 4 to 5 individuals per 100,000 per year in the United States.1 However, their incidence is increasing, likely due to advancements and increased

| | | |
|---|---|---|
| Synaptophysin | : | Immunoreactive cells (3+) in tumor |
| Chromogranin | : | Immunoreactive cells (3+) in tumor |
| NSE | : | Immunoreactive cells (3+) in tumor |
| CD-56 | : | Immunoreactive cells (3+) in tumor |
| Pan CK | : | Immunoreactive cells (2+) in tumor |
| Ki-67 | : | 24 % |

use of radiographic and endoscopic imaging.2 The classification of PanNETs is complex and generally subdivided into either functional (hormone secreting) or nonfunctional. In addition, tumor size and histologic grade, as defined by the proliferation rate, are prognostically important. The majority of PanNETs are nonfunctional and, as a result, frequently go undiagnosed until late in their clinical course. Although PanNETs are typically solid, in rare instances these tumors present as cystic lesions.

Grossly the size vary from 1cm to 18 cm. It is generally assumed that cystic PanNETs are the result of tumor necrosis within solid PanNETs. Thus, they are thought to be similar in biological behavior and malignant potential to their solid counterparts. But conflicting reports suggest that cystic PanNETs represent a distinct entity rather than a morphologic variant. In fact, several studies have found cystic PanNETs to be more frequently associated with multiple endocrine neoplasia type 1 (MEN-1) and less aggressive than their solid counterparts.3-5

Since its original description by Thigpen in 1940,6 subsequent studies have been conflicting as to whether cystic PanNETs represent a distinct biological entity or are formed by necrosis and degeneration. The etiology of cystic PanNETs remains controversial, and several theories have been put forth. 1) Slow-growing PanNETs develop a fibrous capsule that eventually restricts the blood supply to the tumor, resulting in infarction and necrosis. 2) Cystic change or necrosis correlated with large tumor size 3) Hemorrhage within the tumor is the inciting event in cyst development. 4) Alternatively, cyst development may be related to an FNA. 5) Exomic sequencing has identified a subset of PanNETs with recurring mutations in MEN-1, DAXX/ATRX, and the mTOR pathway. Thus, it is not unreasonable to assume that an underlying genetic etiology may be responsible for cystic PanNETs. 7

Cystic PanNETs were typically sporadic (91%), nonfunctional

(91%), solitary (87%), and were discovered incidentally (62%). In comparison with their solid counterparts, cystic PanNETs were more frequently found in the tail (53% vs. 36%). In addition, cystic PanNETs were less likely to demonstrate tumor necrosis, perineural invasion, vascular invasion, regional lymph node metastases, and synchronous distant metastases compared with solid PanNETs. Prognostically, they presented at a lower pathologic stage using both the AJCC and ENETS systems and decreased Ki-67 proliferation index compared with solid PanNETs. However, whether these prognostic predictors are valid for cystic PanNETs remains to be proven 7. Although some studies have reported that cystic PNENs could be identified preoperatively by a hypervascular rim, accurate preoperative diagnosis of cystic PNENs was reported to be only 23% 8. MR may perform better than CT for detecting ductal communication in pancreatic cysts, that usually is not considered as a cystic pancreatic neuroendocrine tumors feature 9. The relatively low resolution of cross sectional imaging compared with EUS precludes the ability to separate cystic PNETs from other cystic neoplasms 10,11

Concurrently, the improvement in endoscopic techniques has allowed nonsurgical sampling and evaluation by endoscopic ultrasound-guided fine-needle aspiration biopsy (EUS-guided FNAB). Due to the high rate of diagnostic accuracy and low rate of complications, EUS has become an integral part of the preoperative assessment of pancreatic cysts. The most important advantage with endoscopic ultrasound is the possibility to obtain tissue and fluid samples from the cysts helpful for the assay of tumour markers such as CEA, enzymes like amylase, molecular markers and cytology. All of these are essential for the achievement of a correct preoperative diagnosis and an appropriate tumor management. 9

The primary difficulty was distinguishing cystic PanNETs from other cystic neoplasms of the pancreas such as IPMN or MCN. As the clinical management for different cystic neoplasms of the pancreas varies, preoperative diagnosis is of utmost importance. Both main duct-IPMNs and MCNs can be associated with an invasive ductal adenocarcinoma.12-14 Recent exomic sequencing of PanNETs has identified a subset of tumors harboring mutations within the mammalian target of rapamycin (mTOR) pathway.15 The mTOR pathway inhibitor, everolimus, has been shown to increase progression-free survival in a subset of PanNET patients.16 Hence, in the future, patients with PanNETs may be treated with targeted therapies inappropriate for IPMNs and MCNs. Since the cystic PanNETs pose diagnostic challenge it is advisable to resect these lesions. Their high resectability rate supports the role of surgical approach and complete resection is actually the treatment of choice for cystic PNETs. Accurate preoperative diagnosis is important for patient management as "watch-and-wait" approach could be highly risky in patients with pancreatic mass lesions. In summary, cystic PanNETs are a distinctive subgroup of PanNETs with unique clinical and pathologic features. Because of their cystic nature, these neoplasms often present a diagnostic dilemma to both the experienced radiologist and pathologist. Awareness and proper recognition of these entities including their associated findings can aid in their diagnosis. Resection is the treatment of choice. Future genetic and molecular studies should help shed light on the pathogenesis and possible treatment strategies for these neoplasms.

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# 99mTC - HYNICTOC SPECT / CT in Detecting Primary Jejunal NET with Liver Metastasis

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Abstract: Neuroendocrine tumors (NET) are a rare heterogeneous group of tumors with an increasing incidence.Cases where histology suggests metastasis from NET without a known primary tumor are categorized as cancer of unknown primary (CUP). CUP patients constitute 7.6-15% of NET study populations.We here report a case of liver metastasis with unknown primary NET detected jejunum lesion using 99mTc-HYNICTOC SPECT/CT .

Key Words: NET, CUP, jejunum, SPECT/CT

Introduction: Neuroendocrine tumors (NET) are a rare heterogeneous group of tumors with an increasing incidence.[1] Arising from the endocrine cells of the diffuse neuroendocrine system of the human body, NET can occur in different body regions.[2] With the density of neuroendocrine cells varying between different body tissues, primary NET are most common in the gastrointestinal tract and in the bronchopulmonary system.[3] Cases where histology suggests metastasis from NET without a known primary tumor are categorized as cancer of unknown primary (CUP). CUP patients constitute 7.6-15% of NET study populations [4], while NET account for less than 5% of all CUP.We report case of unknown primary NET with liver metastasis underwent (99m)Tc-EDDA/HYNIC-Tyr3-octreotide ((99m)Tc-EDDA/HYNIC-TOC)99mTc-HYNICTOC SPECT/CT scintigraphy showing primary jejunal NET.

Case report: A 45 year-old female presented with complaint of abdominal pain in the right side.Ultrasound abdomen showed large lesion in the liver . Biopsy of liver lesion revealed NET. she was referred for whole body 99mTc-HYNICTOC scintigraphy (figure 1) for detecting primary lesion which showed lesion with uptake in the jejunum on SPECT/CT(figure 2) and liver metastasis (figure 3),patient underwent jejunal resection of tumour and liver resection for metastasis.

Discussion: Arising from cells of the diffuse neuroendocrine system, NET primaries can develop in different regions of the body. NET are rare, and only a small proportion of NET patients have cancer of unknown primary.[1,2]However, the true prevalence of CUP in NET patients is likely to be higher due to documentation bias. Bias may result, for instance, when a suspected tumor is documented as a definitive diagnosis.[3,4]

Reported percentages must therefore be interpreted with caution. Identification of CUP by a suitable imaging modality is important because it can markedly improve patient survival. Surgery is the method of first choice in most patients with a locoregionally confined NET primary. Recent data suggest that even patients with nonresectable NET liver metastasis may benefit from resection of the primary tumor.[5]

The sites of NETUP include the bronchi, stomach, duodenum, jejunum, pancreas, colon, and rectum, and different imaging modalities are available to search for the primary.[6]A clear guideline-based diagnostic strategy for identifying NETUP however does not exist. The performance of different imaging modalities in identifying CUP varies with the location in which the tumor is ultimately found. For instance, EUS has excellent detection rates for tumors located in the head of pancreas, while it is naturally not suitable for identifying primaries in the lungs. Somatostatin receptor imaging offers the advantage of enabling whole-body evaluation. It has gained a central role in staging NET.[7]

In-111 DTPA octreotide is the current standard for somatostatin receptor imaging.but in our department ,due to nonavailbility ,we used 99mTc-HYNICTOC for whole body imaging .(99m)Tc-EDDA/HYNIC-TOC is highly indicated for in vivo histological characterization of known NET lesions, previously identified by other imaging modalities or biopsy, to plan appropriate therapy

especially for patients with inoperable disease. Artico et al showed mainly in patients with NET of unknown origin or digestive NETs sensitivity 87%, specificity 86%, positive predictive value 95% negative predictive value 67% and accuracy 87%.[8] some other somatostatin analogs, very similar to 99mTc-EDDA/ /HYNIC TOC have been recently investigated and recommended for clinical use . Some of them are: 99mTc-EDDA- -tricine-HYNIC-NATE, 99mTc-EDDA/HYNIC-octreotate, 99mTc (HYNIC-OC, HYNIC-TOC and HYNIC-TATE) and 111In (DTPA-OC and DOTA-TATE), 99mTc-demotate, 99mTc-P829. Introduction of hybrid systems (SPECT/CT, SPECT/MRI), additionally contributed to the accuracy and clinical validity of this method [9]

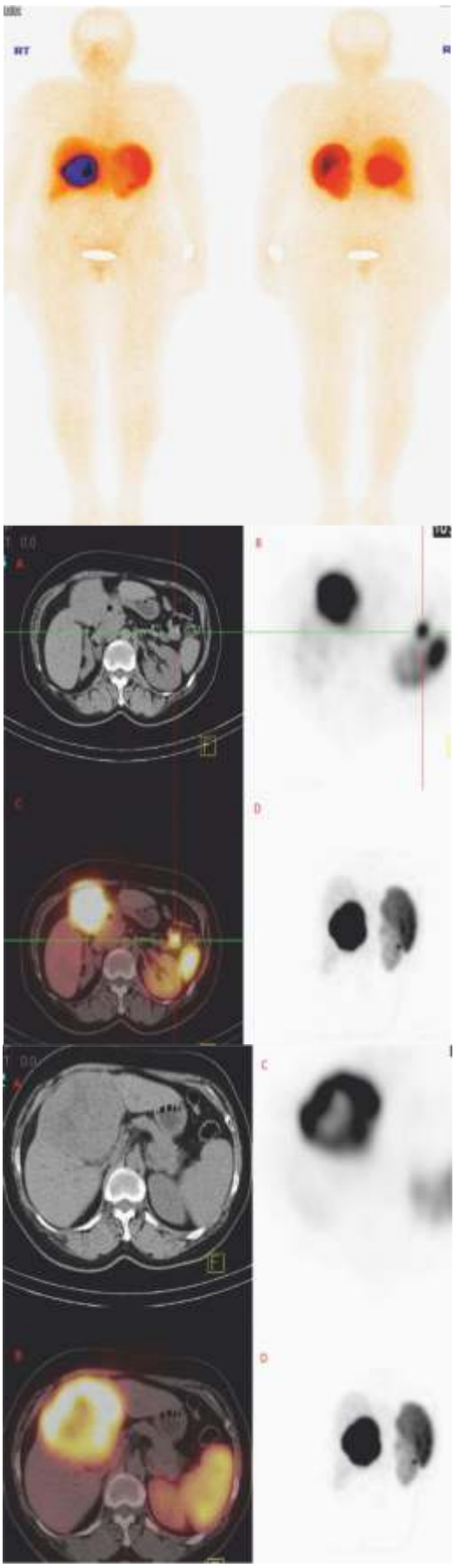
Neuroendocrine tumors (NET) are a rare heterogeneous group of tumors with an increasing incidence.Cases where histology suggests metastasis from NET without a known primary tumor are categorized as cancer of unknown primary (CUP). CUP patients constitute 7.6-15% of NET study populations.We here report a case of liver metastasis with unknown primary NET detected jejunum lesion using 99mTc-HYNICTOC SPECT/CT .scintigraphy (figure 1) for detecting primary lesion which showed

Conclusion: 99mTc-HYNICTOC is useful in identifying unknown primary from liver metastasis.SPECT/CT should be used wherever neccesary to improve sensitivity and localise the lesions .

Figure 1: Whole body 99mTc-HYNICTOC scintigraphy showimg intense uptake in the liver lesion and tiny foci of uptake noted close to left kidney.

Figure 2: SPECT/CT of abdomen localised the uptake near left kidney to the jejunum thickening suggestive of primary site .

Figure 3: SPECT/CT of abdomen showing large lesion in the liver with intense uptake



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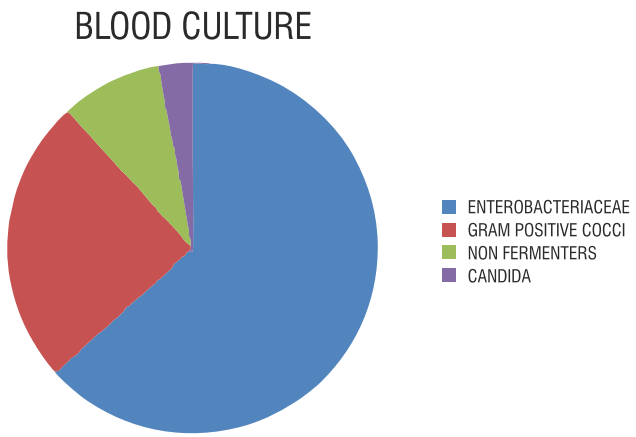
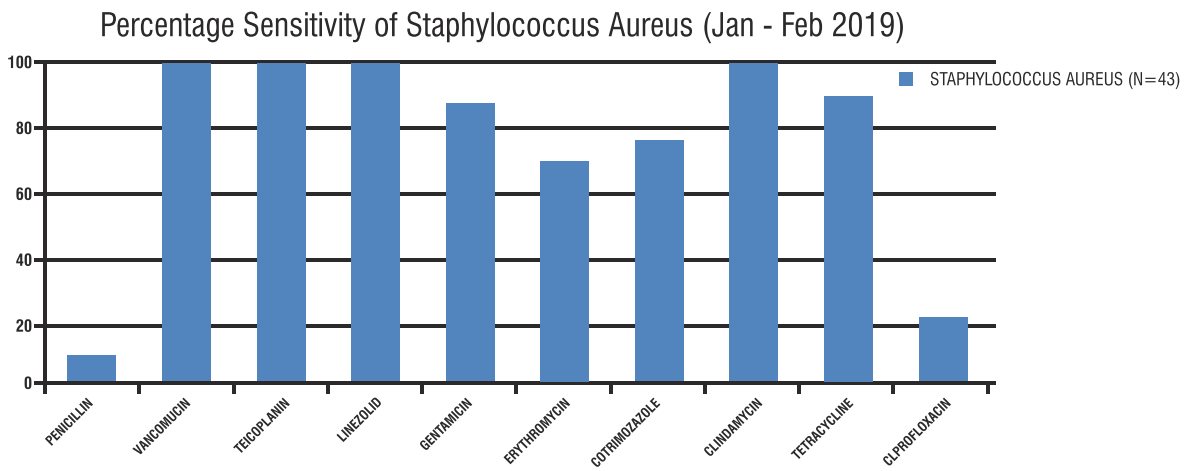
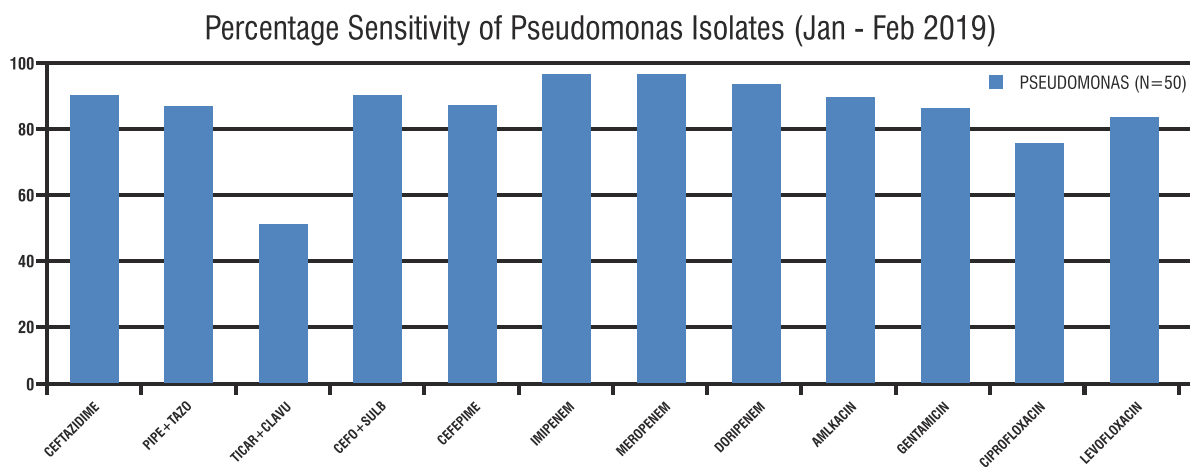
# Community Antibiogram (Jan - Feb 2019)

**(Note: All cultures are from OP patients to reflect the community)**

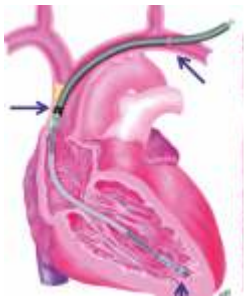



**ENTEROBACTERIACEAE (E COLI - 26, KLEBSIELLA - 12, ENTEROBACTER - 3, SALMONELLA - 2)**
**GRAM POSITIVE COCCI (STAPHYLOCOCCUS AUREUS - 8, STREPTOCOCCUS - 9)**
**NON FERMENTERS (ACINETOBACTER - 3, BURKHOLDERIA - 3)**
**CANDIDA - 2**



## Unique Case of
## Extracting Implanted Heart Wire From Patients Heart - First Case In Coimbatore



Surgically implanted heart devices play an important role in the treatment of heart disease. Pacemakers treat slow heart rhythms by increasing the heart rate. As the range of applications widen, the number of patients with heart devices continues to increase. Occasionally, pacemaker and implanted lead or heart wire must be removed. The removal of such systems is potentially a high-risk procedure. With the increasing number of implanted devices, removal is required more frequently. A pacemaker lead is a special wire that delivers energy from a pacemaker to the heart muscle. A lead extraction is the removal of one or more leads from inside the heart.

Pacemaker leads need to be removed for one or more of the following reasons: Damage to the inside (called a fracture) or outside of the lead. An infection at the site of the device and/or lead. In KMCH, we came across a patient (50 year old female) who had undergone pacemaker implantation for a condition called sick sinus syndrome elsewhere few years ago. Due to infection at the site of pacemaker battery, battery was removed elsewhere. Manual extraction of lead was attempted but failed. She was referred here for lead extraction. If any part of the pacemaker system becomes infected, it is usually impossible to cure the infection without completely removing all hardware from the body. Lead extraction was performed using a special device called the lead locking device by Dr. Lawrance Jesuraj, Electrophysiologist and Interventional cardiologist in KMCH. This is the first case of lead extraction using this device in Coimbatore. It was done under local anesthesia and conscious sedation with heart surgeon was kept standby in case of any major complication. Using this device, lead was extracted safely without any complications. Procedure took approximately 45minutes. Patient was shifted to room the same day and discharged home the next day.

Lead extraction is a complex surgical procedure with some unavoidable risks. Each time the lead is separated from scar tissue; there is a small chance of tearing the surrounding blood vessel or perforating the heart, which can result in major bleeding in the chest or around the heart. In some cases, this requires blood transfusion or even immediate open heart surgery to save the patient's life. In KMCH hospitals we have complete heart care team to handle these kind of complex cases, told Dr M Lawrance Jesuraj, Electrophysiologist at KMCH Hospitals.

## KMCH performs Heart Transplant
## Under the Tamil Nadu Chief Minister's Comprehensive Health Insurance Scheme

Kovai Medical Center and Hospital (KMCH) the pioneer and one of the most successful multi-organ transplant centers in Tamil Nadu. Backed by a team of qualified and experienced doctors, paramedics and state of the art technology, the hospital successfully performing transplant surgeries for Liver, pancreas, heart and kidney for more than a decade.

Sanjay Kumar (name changed), a 26-year-old son of a farmer from Erode district was admitted in KMCH with his heart functioning just about 15%. After studying his health condition, KMCH Cardiology experts Dr. Prashant Vaijyanath and Dr. Sureshkumar, decided that Heart transplant will only be the permanent solution. Last week the Heart transplant surgery was performed with a heart donated from a brain dead person. The transplant surgery was done completely free of cost with the aid of the Tamil Nadu Chief Minister's Comprehensive Health Insurance Scheme

The entire process – right from harvesting the heart from the brain dead person, transporting the organ safe and fast so as to reach the hospital and till the transplant surgery – has to be completed within a short span of time. Time is critical and of paramount importance," said Dr. Nalla G. Palaniswami, Chairman, KMCH. Dr. Nalla G. Palaniswami, Chairman, KMCH, appreciated Dr. Prashant Vaijyanath, cardio thoracic surgeon, Dr.R.Sureshkumar, Interventional Cardiologist and the entire team for performing this transplant procedure which was lifesaving and improved the patient's quality of life. He added that KMCH is equipped with the best expertise and the latest technology to perform any kind of rare and challenging transplant procedures within short notice. Other than heart, KMCH, known as the most successful multi-organ transplant center, also performs kidney, pancreas and liver transplant. He also thanked the Tamil Nadu Chief Minister's Comprehensive Health Insurance Scheme for their timely support and assistance.

## Event & Award Photos


*12th KMCH ICU Update*

*KMCH Cervical Cancer Update 2019*


*AHPI Award 2019*

*Advanced Bronchoscopy Course 2019*


*KMCH Robocon 2019*

## Welcome to KMCH Family

**Dr. P. Santhosh**
*MBBS., MD(Radiology)., FNVIR.,*
Consultant Interventional Radiology
(KMCH - Main Center)

**Dr. Karthiraj Natarajan**
*MBBS., Dip. in Anaesthesiology., DNB (Anaesthesiology)., IDCCM., IFCCM., EDIC.,*
Consultant Intensivist
(KMCH - Main Center)

**Dr. S. Navaneetha Krishnan**
*MD (Pul. Med)., DTCD.,*
Consultant Pulmonologist
(KMCH - Erode Center)

## Upcoming Conference & IMA Details

International Conference on Indian Rural Public Health and Non- Communicable Disesase
Oraganising by: KMCH Researuch Foundation
Saturday, 6th April 2019

Quality Management System in Clinical Laboratory
Oraganising by: Pathology Departmant of KMCHIHSR
Sunday, 21st April 2019

Quality Circle Forum of India (Coimbatore Chapter)
Oraganising by: Quality Council of India
Friday, 31st May 2019

International Conference on Endocrinology
Oraganising by: Endocrinology Department of KMCH
10th & 11th August 2019

Indian Medical Association - Kanyakumari
Topic: 1. Conquering Cancer with Technology - Dr. R. Madhu Sairam
Topic: 2. Life after Transplant - Dr. Paari Vijayaragavan
Saturday, 13th April 2019

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