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EDITORIAL

RADIOMICS: IMAGES ARE MORE THAN PICTURES, THEY ARE DATA

Solid tumors are spatially and temporally heterogeneous. Question is "Can we capture the intratumoral heterogeneity in a noninvasive way". During last decade, medical imaging innovations with new softwares, new imaging agents and newer protocols have allowed the field to move towards quantitative imaging. Radiomics is a novel way of detecting clinically relevant features from radiological imaging data that are difficult for the human eye to perceive.

With high-throughput computing, it is now possible to rapidly extract innumerable quantitative features from tomographic images (computed tomography [CT], magnetic resonance [MR], or positron emission tomography [PET] images). The conversion of digital medical images into mineable high-dimensional data, a process that is known as radiomics, is motivated by the concept that biomedical images contain information that reflect underlying pathophysiology and that these relationships can be revealed via quantitative image analyses. Quantitative image features based on intensity, shape, size or volume and texture offer information on tumor phenotype and microenvironment (or habitat) that is distinct from that provided by clinical reports, laboratory test results, and genomic or proteomic assays. Radiomics appears to offer a nearly limitless supply of imaging biomarkers that could potentially aid cancer detection, diagnosis, assessment of prognosis, prediction of response to treatment, and monitoring of disease status.

The suffix *-omics* is a term that originated in molecular biology disciplines to describe the detailed characterization of biologic molecules such as DNA (genomics), RNA (transcriptomics), proteins (proteomics), and metabolites (metabolomics). The -omics concept readily applies to quantitative tomographic imaging on multiple levels. One multisection or three-dimensional image from one patient may easily contain millions of voxels. Also, one tumor (or other abnormal entity) may contain hundreds of measurable features describing size, shape, and texture. Radiomics analysis epitomize the pursuit of precision medicine, in which molecular and other biomarkers are used to predict the right treatment for the right patient at the right time.

Radiomics offers important advantages for assessment of tumor biology. It is now appreciated that most clinically relevant solid tumors are highly heterogeneous at the phenotypic, physiologic, and genomic levels. In this emerging era of targeted therapies, it is notable that most responses are not durable and that benefit is generally measured in months, not years. For example, this is the case with *(a)* gefitinib in patients with epidermal growth factor receptor–mutated lung cancer, *(b)* trastuzamab in those with human epidermal growth factor receptor 2 (or *HER2*) overexpressing breast cancer, and *(c)* vemurafenib in those with B-Raf–mutated melanoma. Genomic heterogeneity within tumors and across metastatic tumor sites in the same patient is the major cause of treatment failure and emergence of therapy resistance. Thus, precision medicine requires not only in vitro biomarkers and companion diagnostics but also spatially and temporally resolved invivo biomarkers of tumor biology. A central hypothesis driving radiomics research is that radiomics has the potential to enable quantitative measurement of intra- and intertumoral heterogeneity. Moreover, radiomics offers the possibility of longitudinal use in treatment monitoring and optimization or in active surveillance. However, correlation of radiomic data with genomic or other -omic data could inform not only the decision about whether to test for certain gene alterations in biopsy samples but also the choice of biopsy sites. It also could provide confirmatory information to support histopathologic findings. This is important, as it is estimated that the error rate of cancer histopathology can be as high as 23%. Errors in histopathology are due to both sampling errors and observer variability; thus, there is a great need for additional quantitative diagnostic information.

The practice of radiomics involves discrete steps, each with its own challenges. These steps include: (a) acquiring the images, (b) identifying the volumes of interest (c) segmenting the volumes (d) extracting and qualifying descriptive features from the volume, (e) using these to populate a searchable database, and (f) mining these data to develop classifier models to predict outcomes either alone or in combination with additional information, such as demographic, clinical, comorbidity, or genomic data. In the past 10 years, radiomics and radiogenomics research in tomographic imaging (CT, MR imaging, and PET) has increased dramatically. The value of radiogenomics stems from the fact that while virtually all patients with cancer undergo imaging at some point and often multiple times during their care, not all of them have their disease genomically profiled.

Radiomics have been used to automatically compute Gleason grade and were found to enable discrimination between cancers with a Gleason score of 6 (3+3) and those with a Gleason score of 7 of more with 93% accuracy. Seminal radiogenomic studies have shown a relationship between quantitative image features and gene expression patterns in patients with cancer. In patients with lung cancer, there is incontrovertible evidence for intratumoral heterogeneity on lung CT images. These heterogeneities can be captured with features such as spiculation or entropy gradients. Radiomic signature has been used to predict outcome. When gene expression is assessed via pathways, approximately half of the imaging features show strong correlation to genomics. These analyses show that power for predicting gene expression patterns, outcomes, and staging of gliomas can be significantly increased with radiomics-based approaches. Treatment for locally advanced breast cancer suggest that texture analysis of dynamic contrast-enhanced MR imaging can help predict response to neoadjuvant chemotherapy before its initiation. It is axiomatic that images can be used to guide biopsy. They can be used to identify those locations within complex tumors that are most likely to contain important diagnostic, prognostic, or predictive information.

Our vision for radiomics is optimistic and clear. In the foreseeable future, we expect that data gleaned from radiologic examinations throughout the world will be converted into quantitative feature data. To make high-quality data curation a reality, we must first convince the imaging practitioners of its value, and we must streamline the process so it can occur within the limitations of our clinical practice. By playing a crucial role in data curation and analysis of big data, radiologists and physicians alike will be able to make radiomics an important, valuable new dimension of radiology.

Dr. A. K. Dewan
Director - Surgical Oncology

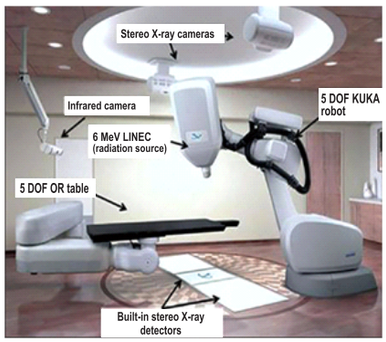
Acknowledgement : Dr. S. Avinash Rao, Director-Radiology

ESSENTIALS OF CYBERKNIFE ---- FOR ONCOLOGISTS WHO DO NOT PRACTICE RADIOTHERAPY

The cyberknife is a stereotactic radiosurgery (SRS) system, comprising of a compact linear accelerator, attached to a highly maneuverable robotic arm, delivering large ablative doses of radiation with utmost pinpoint precision, while minimizing exposure to surrounding healthy tissue.

Most treatment sessions last 30 – 90 minutes depending on the size, shape and location of the tumor.

Concept of Cyberknife



The Cyberknife was invented by Dr. John Adler, a neurosurgeon in Stanford, USA, during the 1990s. Its robotic arm has 6 degrees of freedom of movement, unlike the conventional linear accelerator, which has only rotational movement in one plane. The treatments are non-isocentric, making it possible for the beams to be directed from any desired angle.

The equipment was designed to overcome the limitations innate of the other stereotactic therapy systems by its ability to continually track, detect, and correct for tumor and patient movement even during the treatment.

This system does not require a rigid frame to be fixed onto the patient for stereotactic setup and verification. Initially the machine was used for the treatment of intracranial lesions alone. But subsequent developments extended its indications to most extracranial lesions also, thereby forming a new method of treatment called as **stereotactic body radiotherapy or SBRT**.

Radiobiology of Stereotactic Radiosurgery

The high-dose hypo fractionated irradiation (8–10 Gy per fraction) leads to tumor cell death by:
1. **Direct Cell Kill** : Breaking the double strand in the DNA and killing the cells directly
2. **Indirect Cell Kill** : Indirectly affecting the intra tumor microenvironment through more specific robust endothelial apoptosis and microvascular dysfunction.

Moreover, SBRT impacts disease outside the radiated target too, as the cell death releases enormous amount of tumor antigens that stimulate antitumor T-cell immunity, leading to eradication of occult regional micrometastases and suppressing recurrence and metastatic tumor growth. This is called as the “abscopal effect.”

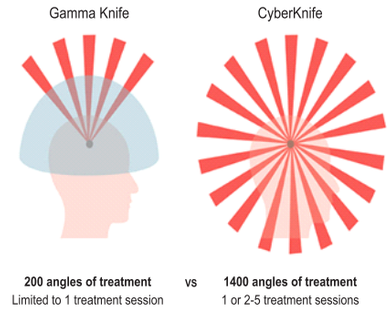
The short radiation duration and high dose per fraction in SBRT have potential radiobiological therapeutic advantages compared with conventional fractionation, due to less proliferation of the surviving clonogenic tumor cells during a fractionated radiotherapy (tumor repopulation). There is also the advantage of less time available for cells to sense and repair radiation induced DNA damage. The accurate and precise delivery of the radiation allows tumoricidal treatment sparing the organ at risk through the differences in radio sensitivity of normal and tumor tissue and through fractionation effects.

Systems of Stereotactic Radiotherapy

With various systems of Stereotactic radiotherapies being in use, like the Gamma Knife, Linear Accelerator based systems, it is important to understand how the CyberKnife is different from the others. The cyberknife has unique features to track the tumor precisely and deliver radiation accurately as desired. While other Linac-based systems have accuracy in millimeters, the CyberKnife boasts of sub-millimeter accuracy in tracking tumor position. Orthogonal x-ray images are taken before each beam and verified for accuracy. Unlike other systems, where treatment is given on a certain fixed phase of breathing (respiratory gating with 4D CT scans), here the robot can move in synchrony with chest movement during breathing and deliver radiation without interruption.

The Gamma Knife has been compared with Cyber knife very frequently, as both these technologies work on the same principles of stereotactic radiosurgery. The Gamma knife has been in use since the 1950s and has more clinical data as evidences. But, there is also a growing body of evidence that shows CyberKnife provides equivalent results for certain tumors and a better outcome for others due to the increased accuracy during treatment as well as not being restricted to one session. The FDA cleared CyberKnife for treatment of tumors throughout the entire body in 2001.

Differences between CyberKnife and Gamma Knife



Gamma Knife requires a large metal frame be mounted onto the patient's head with screws before and during treatment. CyberKnife is a non-invasive and pain-free. Hence, CyberKnife patients require no general or local anesthesia during the procedure, unlike Gamma Knife's.

CyberKnife is a dedicated robotic system that can approach a tumor in the brain, head, neck, and spine from over 1,300 positions with pinpoint sub-millimetre accuracy. Gamma Knife is a gantry-designed system that is limited to 190 positions.

Gamma Knife can only target brain or cervical spine cancer with a single treatment of high-dose radiation, while CyberKnife is able to treat cancer anywhere on the body in one to five radiation treatments.

Salient Differences between the various Stereotactic systems

	CyberKnife	Gamma Knife	LINAC Based
Accuracy	< 1 mm	< 1 mm	5-20mm
Frame needed	No Frame Needed	Required	Immobilization Needed
Fractionation	Yes	No	Yes
Target moving tumours	Yes	No	Yes
Applications	Full Body	No	Yes
Real time Imaging	Yes	No	No (Gating Done)

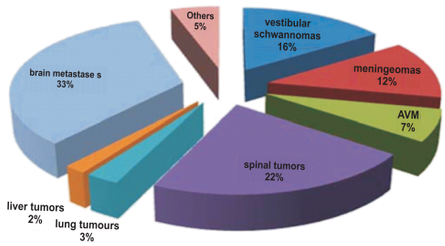
Limitations of Cyberknife

The CyberKnife is not free from limitations. One of the major limitations is the prolonged treatment time: approximately 30 to 60 minutes. This however does not affect the accuracy and precision, since repeated verifications are carried out before each beam delivery. Secondly, large volumes are not suitable for treatment with CyberKnife. This is most suitable for small recurrent and residual tumors after prior radiotherapy treatments.

Scope of Cyberknife

Cyberknife has been used to treat both malignant and benign conditions. The majority of the patients treated have been on palliative settings. But currently there has been an increasing interest for early small volume disease, with a curative intent, like NSCLC, prostate carcinoma, Pancreatic carcinoma, Liver carcinoma, unresectable cancers involving critical structures, residual diseases, recurrent cancers. Some benign conditions that may be treated well with cyber knife are AV malformations, trigeminal neuralgia, acoustic neuroma, meningiomas and pituitary adenomas.

The following diagram shows the indication percentages in a dedicated Cyberknife Centre in Munich.



Indication - percentages of Cyberknife Treatment

Role of Radiology

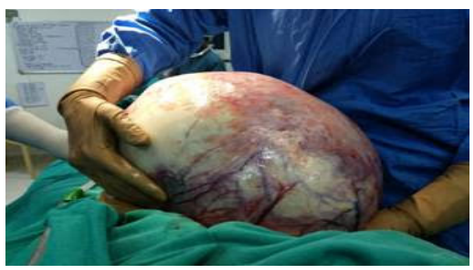
A prerequisite for successful outcomes with the sophisticated Cyberknife, is the close collaboration between imaging experts, pathologists and oncologists. Appropriate imaging studies with CT, PET. MRI is indispensable for accurate, safe and effective treatment delivery. Recently, respiratory motion management has been a challenge in Radiosurgeries. Lesion located at the lung base can move up to 25 mm, while pancreatic and liver lesions can move up to 35 mm during respiratory cycles. 4D CT scans or respiratory motion tracking with the help of fudicials are considered as essential to ensure that the entire target lesion is treated without a substantial increase in the volume of tissue treated. PET-CT has a tremendous impact on diagnostic and post-treatment evaluation by combining anatomic and biological information. However the ideal SUV and evaluation recommendations have yet to be determined.

Conclusion

CyberKnife is a relatively new technology that has been explored as radical and also as palliative treatment modalities in primary and oligometastatic backgrounds. Careful patient selection, high quality imaging studies and multidisciplinary considerations are mandatory in order to achieve the best results.

Dr. Swarupa Mitra
Sr. Consultant & Chief of Gynecological and
Genitourinary Radiation Oncology

HOW TO AVOID CHEMOTHERAPHY IN CANCER PATIENT IF POSSIBLE



58 years old lady, presented to us with severe abdominal distention, loss of appetite of about 2 months duration. On examination, there was fluid in the abdomen but umbilicus was not transverse & there was no shifting dullness.

Contrast enhanced CT scan revealed a large complex Ovarian cyst with all the intestines pushed posteriorly. No free fluid. CA 125 was raised. Patient underwent Ovarian laparotomy, cyst was removed intact & final histopathology was serous carcinoma of ovary stage IA. Patient did not need any further treatment (no chemotherapy).

We must avoid tapping considering it to be ascitic fluid in abdominal distention cases. Contrast enhancing CT scan of abdomen helps in differentiating. Any suspected Ovarian malignancy should not be biopsied unless the patient is sure to undergo chemotherapy. If we do any of the above patients disease gets upstaged to stage IC & Chemotherapy then cannot be avoided.

And we should be aware of the fact that carcinoma in general increases the chances of thrombo embolism and any behavioral changes alert us to this fact, stroke/myocardial infarction/pulmonary embolism.

Take home message

Any complex cyst in ovary whether unilateral or bilateral if CA 125 is raised, biopsy should not be taken from the ovary.

Dr. Leena Dadhwal
Consultant – Surgical Oncology

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CONGRATULATIONS TO DR. RUPINDER SEKHON

Indian College of Obstetricians & Gynecologists (ICOG) felicitated Dr. Rupinder Sekhon, Sr. Consultant & Chief of Gynae Oncology with Fellowship Award in 62nd All India Congress of Obstetrics & Gynaecology – AICOG 2019 on Friday, 11th January 2019 at Gayatri Vihar, Palace Grounds, Bengaluru.

ASOCON 2019 - 4TH ANNUAL NATIONAL CONFERENCE OF ANAESTHESIA SOCIETY FOR OBESITY

RGCIRC participated in 4th Annual National Conference of Anaesthesia Society for Obesity held on 11th to 13th January 2019 at Ahmedabad, Gujarat. Dr. Shikha Modi from Anesthesia (1st Year DNB Resident) delivered an oral presentation on "Respiratory Implications in Morbidly Obese Patient in Major Robotic Neobladder Surgery" which was co-authored and moderated by Dr. Itee Chowdhury, Sr. Consultant – Anaesthesiology.

CME – IMA JANAKPURI

RGCIRC organized a CME in association with IMA Janakpuri on Saturday, 2nd February 2019 at IMA Medico House, Janakpuri, New Delhi. Dr. Sandeep Jain, Sr. Consultant – Pediatric Hematology Oncology delivered a lecture on "Approach to a Child with Suspected Cancer" and Dr. Abhishek Bansal, Consultant – Interventional Radiology spoke on "Interventional Radiology – Treatment Paradigms to Help Your Patients" in the said CME.

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