NEWSLETTER - AONEI

DARPAN: A Reflection of AONEI Activities

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EDITOR'S NOTE

With the blessing of all of the members the newsletter has now entered into the 2nd year. The 1st newsletter was published last year at Gangtok Annual conference and got a very good response from the members and other doctors. I sincerely thank all the members of AONEI fraternity and people who are contributing for publishing the newsletter periodically. But this should continue without any interruption and it will be possible with support from all of you only.

Last year AONEI conducted academic meetings at Guwahati, Imphal, Jorhat with the participation of AONEI members and invited faculties from India and abroad also.

Besides the academic activities AONEI is also doing Community and Social work as per its aims on regular basis. Members are actively getting involved in cancer awareness programmes, Talk shows on TV. Radio talks, health camps etc etc. on a regular basis. Last year AONEI had conducted awareness camp at Nalbari, TV show at Guwahati, and other places. These activities has increased the public awareness regarding the cancer.

Technology is important part of evolution and future, AONEI has also taken a step into the world of technology. AONEI has also achieved a new milestone this year. From February 2016 the new dynamic and user friendly AONEI website is launched (www.aonei.in). The website is active now and I hope the members will be interested in making the website a successful platform for the academic. and interactive work. Members can also initiate blog with group discussion on various topics. The members can send their inputs or enquiry at the official mail address of the site aonei_secretary@aonei.in. .

This year we are going to meet again at Imphal during the annual conference and surely will continue the encouragement and work in future also.

Long Live AONEI

Dr. Vikas Jagtap
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1st News Letter launch by - Mr. AK Ghatani (Hon' Health Minister, Sikkim)
Dr. Kumar Bhandari (Secretary cum DGHS, Sikkim)
Annual Conference – GANGTOK - 2015

NEOADJUVANT THERAPY IN RESECTABLE OESOPHAGEAL CANCER

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Esophageal cancer is the most rapidly Increasing tumor type in the developed world. Globally, esophageal cancer is eighth most common and sixth most fatal malignancy. The lifetime risk, as well as histology of esophageal cancer varies worldwide from 1 in 200 in the US, with more than half of new case being adenocarcinoma (AC) of the lower esophagus or gastro esophageal junction to more than 10 times that risk in India, Iran, Northern China and Southern Africa, where the histology is >90% squamous cell carcinoma (SCC).

Despite improvements in surgical and radiotherapy (RT) techniques and refinements of chemotherapeutic regimens, long-term survival, even from localized esophageal cancer, remains poor. Treatment paradigms differ between western and Asian countries, but the unifying theme that has emerged in the past decade implies that surgery alone can no longer be considered the standard of care. Outcomes in patients with locoregional resectable esophageal cancer have slightly improved since incorporation of multimodality therapy in the treatment of these patient populations.

AC and SCC are the two principle variants and account for >98% of esophageal cancer diagnoses. Historically, AC and SCC have been treated as a single disease entity. Over the year, however, an increasing number of evidence has been accumulated to support the notion that AC and SCC represent two separate diseases based on their differing etiology, epidemiology, prognosis and response to treatment. Epidemiologically, there has been a dramatic shift in the two histologies. Incidence of AC of the esophagus is rising worldwide, whereas the incidence of SCC is decreasing.

Multiple clinical trials have addressed the preferred treatment sequence in managing locally advanced esophageal cancer; however, no standard therapy has been established. While esophagectomy remains the cornerstone treatment of clinically localized disease, the systemic nature of the disease attributes to the failure of surgery alone. Systemic chemotherapy, with or without radiotherapy, could lead to improved outcomes. Several trials has addressed the role of chemotherapy and radiotherapy, before and/or surgery; however, with conflicting results. Surgical resection remains the standard treatment in early stage disease. In surgery-only series, 5-yr survival rates were less than 50% for patients with stage II or higher disease. Therefore, it is recommended that patients with locally advanced disease (T2 or greater or node positive) receive neoadjuvant therapy (chemotherapy or chemoradiation).

Several randomized trials comparing neoadjuvant radiotherapy and surgery vs surgery alone in patients with locally advanced esophageal cancers have been reported. No statistically significant difference was seen in overall survival (OS) with preoperative radiotherapy compared with surgery alone.

Multiple randomized controlled trials (RCTs) compared preoperative chemotherapy and surgery with surgery alone for the treatment of resectable esophageal cancers. Of the seven earlier trials, four showed no survival benefit to neoadjuvant chemotherapy and three did show a survival benefit with neoadjuvant chemotherapy compared with esophagectomy alone. Larger, more recent studies have shown improved benefits for patient receiving neoadjuvant therapy. In the Medical research Council (MRC) study, the overall survival rate was significantly improved in the perioperative chemotherapy arm (36% vs 23%) in patients with resectable AC of esophagogastric junction or lower esophagus.

A meta-analysis published in 2002 included 11 RCTs comparing surgery alone with preoperative chemotherapy, however, showed no statistically significant difference in 3-year survival in patients who received preoperative chemotherapy compared with those who underwent upfront surgical resection. Two additional meta-analyses demonstrated survival benefits for preoperative chemotherapy; the first was a Cochrane review, which pooled 11 randomized trials. A statistically significant difference in survival favoring preoperative chemotherapy was detected only at 5 years. An updated meta-analysis comparing survival after neoadjuvant chemotherapy or surgery alone in 9 RCTs for resectable esophageal cancer found strong evidence of a survival benefit to neoadjuvant chemotherapy over surgery alone, with an absolute survival difference at 2 years of 5.1%.

The poor outcome associated with surgery alone and the high locoregional tumor recurrence rate with definitive chemoradiotherapy provided the rationale behind evaluation of neoadjuvant chemoradiotherapy in patients with resectable esophageal cancer. At least 10 RCTs compared neoadjuvant chemoradiotherapy followed by surgery with other modalities. The Irish trial and the Dutch trial (CROSS study) showed statistically significant improvement in OS with combined preoperative chemoradiotherapy, and an unusually poor survival rate in the surgery-alone arm.

Several meta-analyses have addressed the benefit of trimodality therapy over surgery alone for esophageal cancer. The first meta-analysis by *Fiorica et al* pooled six RCTs comparing preoperative chemoradiation and surgery with surgery alone. Chemoradiotherapy followed by surgery significantly decreased mortality; however, the risk of postoperative morbidity was higher in the multimodality arm.. The most recent meta-analysis, by *Sjoquist et al*, included 12 RCTs of neoadjuvant chemoradiotherapy vs surgery alone, where a survival benefit was evident for neoadjuvant chemoradiotherapy but was not statistically significant.

A meta-analysis of the two trials (an Australian trial and POET trial) comparing neoadjuvant chemotherapy with neoadjuvant chemoradiotherapy favored chemoradiotherapy, but it was not statistically significant

The majority of the previously mentioned studies found that pathological complete response (pCR) in the surgical specimen indicated a better overall outcome, which may make it tempting to intensify preoperative therapy by increasing the number and potency of chemotherapeutic agents and/or radiation therapy (including targeted therapy). Patients with no response fared worse in terms of 5-year overall and disease-free survival rates. Additionally, patients achieving a pCR were more likely to have an R0 resection compared with a partial pathological response or surgery alone.

Conclusion: Management of resectable esophageal cancer has undergone a major evolution over the past two decades. Patients with higher than T1 or node-positive disease who are surgical candidates should undergo some form of neoadjuvant therapy prior to surgery, based at least on the findings of the recently published Dutch trial. In this trial, patients who received neoadjuvant chemoradiotherapy had a median overall survival of 49.4 months, compared with 24 months in the surgery-alone group.

The optimal neoadjuvant treatment regimen has not been established. Most of the institutes use platinum-based combination therapy rather than single-agent therapy (continuous infusion or weekly paclitaxel/carboplatin regimen) concurrent with radiation therapy. Treatment decisions for individual patients should be based on comorbidities and the effects of neoadjuvant therapy on the patient's performance status and quality of life. Incorporating targeted therapy into neoadjuvant treatment based on tumor profiles will help identify patients who may be likely to benefit from certain treatment modalities, which may improve outcomes in this disease.

References:

1. Medical Research Council Esophageal Cancer Working Group. Surgical resection with or without preoperative chemotherapy in esophageal cancer: a randomized controlled trial. *Lancet*. 2002; 359 (9319); 1727-1733.
2. *Cunningham D, Allum WH, Stenning SP, et al*. Perioperative chemotherapy versus surgery alone for resectable gastro esophageal cancer. *N Engl J Med*. 2006; 355(1): 11-20.
3. *Urshcel JD, Vasan H, Blewett CJ*. A meta-analysis of randomized controlled trials that compared neoadjuvant chemotherapy and surgery to surgery alone for resectable esophageal cancer. *Am J Surg*. 2002; 183(3): 274-279.
4. *Sjoquist KM, Burmeister BH, Smitthers BM, et al*. Survival after neoadjuvant chemotherapy or chemoradiotherapy for resectable esophageal carcinoma: an updated meta-analysis. *Lancet Oncol*. 2011; 12(7): 681-692.
5. *Walsh TN, Noonan N, Hollywood D, et al*. A comparison of multimodal therapy and surgery for esophageal adenocarcinoma. *N Engl J Med*. 1996; 335(7): 462-467.
6. *Van Hagen P, Hulshof MC, van Lanschot JJ, et al*. Preoperative chemoradiotherapy for esophageal or junctional cancer. *N Engl J Med*. 2012; 366(22): 2074-2084.

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SINONASAL TERATOCARCINOSARCOMA- A CASE REPORT

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Teratocarcinosarcoma is a rare aggressive malignant tumor charecterized by complex admixture of teratomatous and carcinosarcomatous component. In literature different names have been documented, such as blastoma, malignant teratoma and teratocarcinoma. First reported case was by Shanmungaratnam (1983) et al. under the term "teratoid carcinosarcoma. It often tends to occur in the nose, pharynx and sinus areas, but tumor in other parts of the body has also been recorded. Clinical features are determined by the size and location of the tumor. The most common complaints at presentation include nasal obstruction, epistaxis, facial pain, headache, proptosis and visual field deficits. This neoplasm is more commonly seen in male with male to female ratio 4:1 and in age group between 18-79 year. They are locally aggressive and highly recurrent tumor.

Less known about their metastatic potential except very few reports mentioning about metastasizing to regional lymph nodes as well as in the lungs.

Main mode of treatment is surgical resection with post operative radiotherapy with or without chemotherapy.

Here, we report a case of 72 year old male from dibrugarh presented with complaints of epistaxix, nasal blockade for past 5-6 months. His CT report was given as inflammatory sinonasal disease with polyposis at places including left sided nasochoanal polyp . The patient was operated outside for polypectomy and biopsy was sent to our hospital.

Histopathology sections showed fragments of upper respiratory mucosa with ciliated columnar lining admixed with fragments of tumor composed of benign and malignant counterparts of both epithelial and mesenchymal components in variety of histologic patterns . There are sheets of densely–packed small cells with scanty cytoplasm and uniform rounded nuclei resembling undiferentiated blastemal cells with proliferative neuroepithelium in the form of tubules. Also noted were the charecteristic squamous epithelium with "fetal-type" clear cells, areas of necrosis and increased mitosic figure. Immunohistochemistry demonstrated positive staining for cytokeratin, epithelial membrane antigen, vimentin, synaptophysin, S-100, chromogranin, GFAP and CD99. This polyimmunophenotypic characteristic and diverse histological differentiation provided basis for the diagnosis.

Diferential diagnosis includes Poorly differentiated carcinoma, sarcoma and olfactory neuroblastoma.

Now patient is undegoing radiation therapy. Knowing its highly aggressive behaviour, patient will be closely followed up and chemotherapy may be integrated as an adjuvant or palliative setting.

References

1. Kazemian A, Manshadi H.R. D, Kermani S.Sinonasal Teratocarcinosarcoma; Report of a case. Iran. J. Radiat. Res., 2004; 2 (3): 159-2
2. Shanmugaratnam K, Kunaratnam N, Chia GS, Sinniah R. Teratoid carcinosarcoma of the paranasal sinuses. Pathology 1983;15::413-9
3. Sharma H.S., Abdullah J.M., Othman N.H., Mohmamad M. (1998).Pathology in focus.Teratocarcinosarcoma of the nasal cavity and ethmoid. J. Latyngo. Otol., 112:682-6

Fig1. H&E, 20x-nests of primitive neuroectodermal tumor cells with overlying fetal type clear epithelium

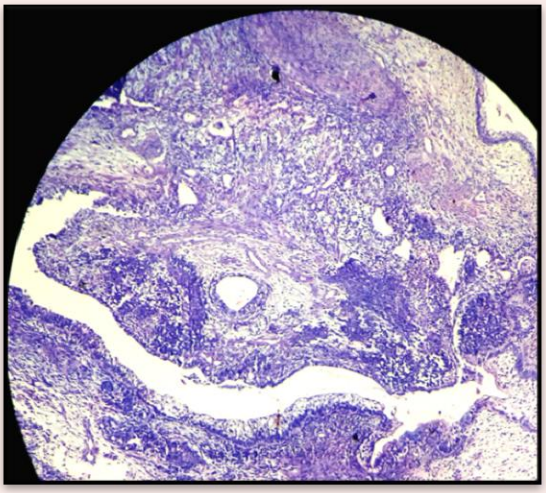
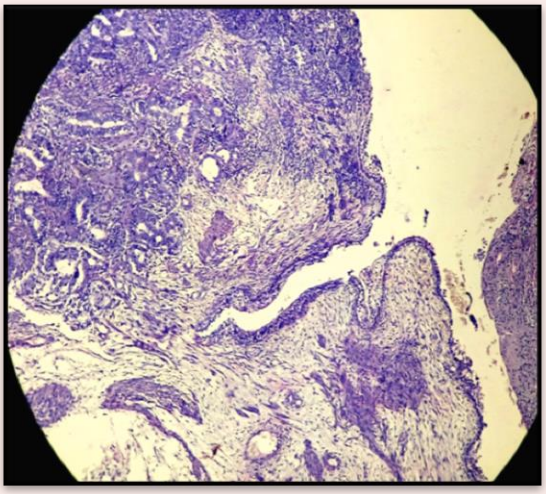


Fig 2. H&E, 20x-epithelial glandular carcinoma and sarcomatous component



GUEST COLUMN

THE ROLE OF STEREOTACTIC BODY RADIOTHERAPY IN NON SMALL CELL LUNG CANCER

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General aspects:

Carcinoma lung is the most common cause of cancer and mortality worldwide. Nearly 1.4 million new cases of lung cancer are diagnosed every year. [1]. The traditional management of early non small cell lung cancer (NSCLC) carcinoma lung patients is surgery. It should be noted that even in early disease, 20-30% of patients are inoperable because of their co morbidities [2] Traditionally, these inoperable patients received conventional radical radiotherapy and had relatively poor 2 year survival rates ranging from 20-30% [3].

Stereotactic body radiotherapy (SBRT) is a high precision technique of radiation therapy. This evolved from stereotaxy treatment of cranial sites which evolved in 1950's with the advent of gamma knife. However, this technique is now being used for extra-cranial sites as well, including lung neoplasm and liver metastasis [4]. In the case of NSCLC, the advantages of high precision and shorter overall treatment duration with this technique have translated into improved control and survival rates as well, as compared to conventional and radiotherapy [5,6].

Stereotactic Body Radiotherapy (SBRT)

Stereotactic Body RadioTherapy (SBRT) [or Stereotactic Conformal RadioTherapy (SCRT) or Stereotactic Ablative Body Radiotherapy (SABR)] combines the advantages of image guidance, highly conformal and highly hypo-fractionated radiation dose delivery to treat tumors over a short time. One of the first clinical experiences was initiated at Karolinska University hospital, Sweden in 1991 and was closely followed by Japan in 1994 [4]. This technique not only decreased the duration of treatment but also matched the survival rates of surgically treated patients [5,6].

Patient selection

Most patients who have received SBRT in various studies had T1 or early T2 lesions with no mediastinal or systemic metastasis. Earlier studies included only peripheral disease patients for SCRT since there were reports of severe complications for patients with central lesions. However, now there is emerging literature for treating central lesions closer to the mediastinum as well. However, it is to be noted that it is appropriate to avoid high dose fractions when tumours are close to the mediastinum.

SBRT literature:

No phase III randomized study has been reported so far with a parallel design of conventional versus hypo-fractionated SCRT in NSCLC. There are a large number of prospective and retrospective studies assessing the role of SCRT in carcinoma lung [7-9]. Most of the studies included early stage tumors (5–6 cm), with very few including T3, metastatic and even recurrent lesions; primarily which were inoperable due to medical reasons. The age group of subjects ranged from 50 to 78 years (median); with follow-up ranging 11 to 90 months (median). In all, more than 1800 patients have been treated in various studies. The majority of them have been single institutional trials. The number of patients per study has varied from 30- 250. The dose delivered and fractionation has varied from 15 Gy in single fraction (#) to 70 Gy/10#. The commonly used dose fractionation schedules are, 60–66 Gy/3#, 45 Gy/3#, 40 Gy/4#, 48 Gy/4# and 50–60 Gy/5-6#. Usually, not more than 3 fractions are delivered per week (alternate day treatment schedule). However recent literature does not report excess complications with daily treatment schedule.(10) Efforts are also on to make SBRT a single fraction treatment, and this would be a remarkable achievement indeed.(11) Currently, the overall 3 year survival rates with SBRT have ranged between 50-70% with local control rates of >85% in most series. It is to be noted that most patients currently being treated with SBRT are the ones who are unfit for surgery and therefore have significant comorbidities. These comorbidities themselves are a risk factor for survival of these patients.

Summary

SCRT has shown promise in the management of early NSCLC patients with poor performance status. These results have closely matched the results obtained by surgical resection. SCRT thus heralds a paradigm shift in management of early stage lung cancer, presenting the option of effective treatment by a simple non invasive technique.

References:

1. J. Ferlay, F. Bray, P. Pisani et al., GLOBOCAN 2002: Cancer incidence, mortality and prevalence worldwide, in IARC CancerBase, IARC Press, Lyon, France 2009.
2. R. Rami-Porta, D. Ball, J. Crowley. The IASLC lung cancer staging project: Proposals for the revision of the T descriptors in the forthcoming (seventh) edition of the TNM classification for lung cancer, J Thorac Oncol. 2007;2: 593–602.
3. X. Qiao, O. Tullgren and I. Lax, The role of radiotherapy in treatment of stage I non-small cell lung cancer, Lung Cancer. 2003;41:1–11
4. Munshi A, Krishnatry R, Banerjee S, Agarwal JP.Stereotactic conformal radiotherapy in non-small cell lung cancer - an overview.Clin Oncol (R Coll Radiol). 2012 ;24:556-68
5. Oshiro Y, Aruga T, Tsuboi K, and et al. Stereotactic body radiotherapy for lung tumors at the pulmonary hilum. Strahlenther Onkol. Epub 2010 Apr 26
6. Onishi H, Kuriyama K, Komiyama T and et al. Clinical outcomes of steriotactic radiotherapy for stage I non small cell lung cancer using a novel irridiation technique: patient self-controlled breath –hold and beam switching using a combination of linear accelerator and CT scanner. Lung Cancer. 2004;45:45-55.
7. Neal E. Dunlap, James M, Paul W et al. Size matters: A comparison of T1 and T2 peripheral non–small-cell lung cancers treated with stereotactic body radiation therapy (SBRT). Thorac Cardiovasc Surg. 2010;140:583-589.
8. Y. Chen, W. Guo, Y. Lu and B. Zou, Dose-individualized stereotactic body radiotherapy for T1-3N0 non-small cell lung cancer: long-term results and efficacy of adjuvant chemotherapy. Radiother Oncol. 2008;88:351–358.
9 Michael T M, Louis S C, Paul O. Normal Tissue Tolerance Dose Metrics for Radiation Therapy of Major Organs. Semin Radiat Oncol. 2007;17:131-140.
10 Stauder MC, Macdonald OK, Olivier KR, Call JA, Lafata K, Mayo CS, Miller RC, Brown PD, Bauer HJ, Garces YI. Early pulmonary toxicity following lung stereotactic body radiation therapy delivered in consecutive daily fractions. Radiother Oncol. 2011 ;99:166-71.

11 Videtic GM, Stephans KL, Woody NM, Reddy CA, Zhuang T, Magnelli A, Djemil T. 30 Gy or 34 Gy? Comparing 2 single-fraction SBRT dose schedules for stage I medically inoperable non-small cell lung cancer. Int J Radiat Oncol Biol Phys. 2014 ;90:203-8.

Growing Teratoma Syndrome: A Brief Communication

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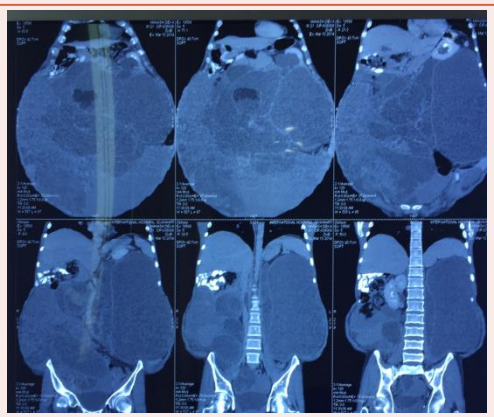
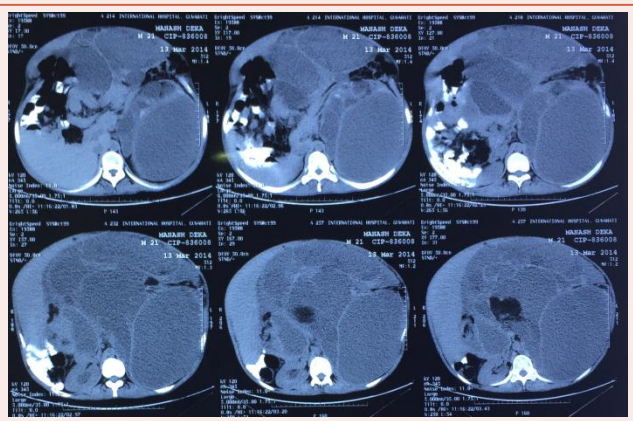
Growing teratoma syndrome (GTS) is defined as an increase in tumour size during or aftern chemotherapy for germ cell tumour (GCT), with mature teratoma at histological analysis of the resected tumour specimen. GTS should be suspected in patients with: (1) metastatic NSGCT, (2) increasing size of metastatic lesions on serial imaging during or after systemic chemotherapy for the treatment of testicular cancer and (3) normalized serum tumor markers. The diagnosis is confirmed by the presence of mature teratoma and the absence of any malignant germ cells on final surgical pathology. Good treatment outcomes are dependent on the following five steps: (1) awareness of this condition, (2) vigilant imaging of patients on chemotherapy for NSGCTs, (3) early recognition of the paradoxical response of disease to chemotherapy (enlarging tumors and normal serum tumor markers), (4) early diagnosis and, finally, (5) a prompt and complete surgical resection of tumors. We report a case of GTS treated with complete surgical resection.

A 22-year-old boy presented with history of right testicular germ cells tumour treated with orchidectomy and adjuvant chemotherapy. After 3 years of treatment, the patient developed progressively growing abdominal mass with normal tumour markers. During the course, he received multiple chemotherapy in different hospital without any clinical response before coming to me. As per the protocol of treatment of GTS, complete surgical resection of the tumour was done and the patient recovered postoperatively without any complication and there was no recurrence of the disease after one-year follow-up. Final histopathology report showed mature teratoma. Awareness of this syndrome is necessary to prevent unnecessary chemotherapy and allow optimal management.





AONEI : EVENTS AND ACTIVITIES

Annual Conference - GANGTOK

Breast Cancer Symposium
Imphal (Manipur)

Nalbari
Cancer
Awareness
Camp

Breast CME
Guwahati

Press meet
Guwahati

AONEI : EVENTS AND ACTIVITIES

Annual Conference - GANGTOK
Inauguration by Mr. AK Ghatani (Hon' Health Minister, Sikkim)
Dr. Kumar Bhandari (Secretary cum DGHS, Sikkim)

Souvenir launch
Annual Conference – GANGTOK - 2015

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UPCOMING EVENT

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Hotel Classic Grande : 20th & 21st Feb 2016
Imphal (Manipur)
Organizing Secretary: Dr. Y Indibor Singh
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CME and Surgical Workshop
BBCI, May 2016
Organised by
FHNO & Dept. of Head and Neck Oncology,
BBCI, Guwahati

Workshop & CME on VATS !9th March 2016
Organised by: Department of Surgical Oncology
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NE – AROI Zonal Chapter Annual Conference
October 2016
Dimapur (Nagaland)
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CME: Head & Neck Cancer
And Cyberknife Talk
Hotel Gateway Grandeur, Guwahati
12th March 2016