



NEWSLETTER - AONEI

Official Publication

Association of Oncologist of North East India : Volume 1; Issue 1: 2015

Message From Founder Members

AONEI EVOLUTION

It was 2004, the idea of AONEI was mooted on the breakfast table at Hotel Pinewood, Shillong by myself, and Dr. Judita Syiemlieh (Consultant Radiation Oncologist, Civil Hospital, Shillong). It was decided to convene a meeting of all the working oncologist of the region and finally it happened with an evening scientific programme at Hotel Polo Tower in Shillong in December 2004. With the support of 20 oncologist ANOEI was formed. The core committee members were myself, Dr. Judita Syiemlieh, Dr. P K Choudhury, Dr. S B Medhi and Dr. M N Barua. The constitution for the organisation was drafted and placed in a general meeting held in July 2005 at Hotel Landmark, Guwahati. The first executive committee was formed with Dr. S B Medhi as President, myself as Secretary, Prof. T H Tomcha Singh as Vice President and Dr. Judita Syiemlieh as Asst. Secretary. Registration of the society, finding the logo and making of stationeries followed.

The first conference of AONEI was held in March 2006 at Hotel Progoti Manor with a theme of Head and Neck cancers with eminent speakers from all over India. It was decided in the general meeting that cancer awareness amongst public and amongst practicing doctors is equally lacking and we decided to take up satellite scientific meetings at different places covering the North Eastern States(5-6 meetings every year).

During my tenure of 6years (3 terms) meetings were held at Guwahati, Shillong, Cherapunjee, Jowai, Silchar, Aizawl, Itanagar, Imphal, Agartala etc. Collaborations were made with Neurosurgeons, Association of Surgeons of Assam, Oncologists, Physicians, Hematology Group, Gynaecologists to have focused meetings and these were held at Guwahati with good participation.

Now the AONEI is taking strides in the hands of our young Oncologists and I feel that the organization is maturing and will go ahead spreading awareness about cancer and its treatment both amongst public and practicing doctors in the region.



Dr. C Bhuyan
Professor & Head
Department of Medical Oncology
BBCI, Guwahati – 16

MESSAGE FROM FOUNDER PRESIDENT

It gives me deep sense of satisfaction when I came to know from Dr. Vikas Jagtap, Radiation Oncologist that the AONEI is going to publish its first 'NEWS LETTER' this year, at the annual conference in Sikkim.

The AONEI was formed with only 20 members from different North Eastern States about 10 years back in 2005. its first Inaugural Annual meeting was held in 2006, at Guwahati. The Association has so far performed a commendable job by exchanging scientific and academic knowledge among the Oncologists of North East India by holding Workshops, Seminars & Discussion etc. to keep pace with the recent advances, at par, with the rest of the country.

Further, I am extremely proud of the members for taking extra efforts to create awareness for the prevention, early detection & management of cancer among the people of the North Eastern states by holding meetings, displaying posters, film shows and through the electronic media etc.

Since cancer is a killer disease and its occurrence is more in North east than rest of India, it is my humble request to all members to involve in active cancer research to find out the cause and get to the root of the problem. So, the association has to cut out a road map towards this end. I would further request all to keep abreast of the latest know how and techniques to equip themselves for the future prospects and reputation of the organisation,

Finally my sincere thanks to each and every member for their help, guidance and cooperation they have extended for the past decade.

May god bless every member with health and happiness.

LONG LIVE AONEI



Dr. S B Medhi
Founder President
AONEI, Assam
Consultant Surgeon, ENT

PRESIDENT MESSAGE

The Association of Oncologists of North east India (AONEI) has come a long way since its formation in 2005, progressing step by step in enhancing, improving and building a strong professional platform for comprehensive cancer care. The ability to share knowledge, skills and expertise allows us to continuously keep up with developments in our field. This bears a direct impact on patient care as we all strive to make cancer care available and accessible especially to those who would find it difficult to travel long distances for medical help. Future directions of the Association would include collaborative work, training, research and publications. We are happy to bring out this newsletter. The Editorial Board has put in a lot of effort. We welcome your suggestions for the forthcoming newsletters and for the thrust areas of the Association.



Dr. Ravi Kannan
Director
Cachar Cancer Hospital &
Research Centre

EDITOR'S NOTE

It gives me immense pleasure to give you all the first AONEI newsletter. Now in the era of evidence based medicine, I hope that this newsletter will be a great platform for the academic forums in the north east region. It will also serve the purpose of information about the members, their achievements, meetings and activities of AONEI.

But any organization will see the sky only when the members provide their inputs in the academics, scientific programmes, meetings and other activities of AONEI.

We are planning to do a biannual publication of the newsletter and if it succeeds we may make it quarterly issue, but of course not without the support of all of you. We have already taken a leap into the future. I wish all the members work in hands for the further progress of AONEI. Hope we all grow with our association.



Dr. Vikas Jagtap
Asst Professor
Department of Radiation Oncology
BCCI , Guwahati - 16

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- Dr. J N Buragohain, Secretary, AONEI; jadunathbg@yahoo.co.in
- Dr. Vikas Jagtap, Editor, AONEI; drvikasj@yahoo.co.in
- *Data published in this issue is for academic purpose only and should not be considered as a standard reference.*

SECRETARY MESSAGE

Dear esteemed members

It is indeed a moment of pride and pleasure that this newsletter is being released at last. All credits goes to Dr Vikas Jagtap. Through this news letter at the very outset I offer my sincere thanks to the president, executive members and members of AONEI for giving me the opportunity to serve as the secretary of the association and being supportive all throughout.

As a new initiative of our association, this news letter should be one of the medium through which our association's events and activities should be highlighted. I would like to request our members to contribute articles, news, academic updates and their achievements.

Looking back it is indeed a great moment for AONEI which has completed 10 glorious years. I am thankful to the founder members of AONEI, viz founder President and Secretary and host of past president and dedicated members who have been instrumental in carrying forward the legacy of AONEI.

I would also like to welcome all the members and delegates for our 10th annual conference of AONEI, to be held in the beautiful capital of Sikkim (Gangtok) on 4th and 5th April 2015.

Friends, change is the only constant in human life. We need to change with the time to progress as individuals and as an organization. I hope good work will be carried forward by other esteemed members. I am hopeful for our association's future and wish everyone all the best for the upcoming events.

Long live the "Association of Oncologists of North East India".



Dr J N Buragohain
Consultant Oncosurgeon
Secretary, AONEI , Guwahati



Dr Rajjyoti Das, Asst. Prof, Dept of Head & Neck Oncology, BBCI

Dr Partha Sarathi Chakraborty, PG Fellow, Dept of Head&Neck Oncology, BBCI

Dr Kaberi Kakati, PG Fellow, Dept of Head & Neck Oncology, BBCI

Dr Rubu Sunku, Registrar, Dept of Radiation Oncology, BBCI

Introduction –

Ameloblastic fibrosarcoma (AFS) is a rare odontogenic malignancy with benign epithelial and malignant ectomesenchymal components. Till date, around 66 cases have been reported in the medical literature. AFS has a predilection for the mandible; and it is most commonly seen in the third decade of life with a male preponderance. Metastasis is rare, but recurrences have been reported.

We report here a case of ameloblastic fibrosarcoma originating in the mandible in a 21 yr old male.

Case report –

A 21 yr old Muslim male, cultivator by profession, hailing from Sonitpur, presented at the Head & Neck OPD of Dr. B. Borooah Cancer Institute with a 8 yr history of gradual swelling of face and oral cavity. Extraorally, the swelling involved the chin and left side of lower face, measuring approx 10cm x 8cm. Intraorally, it involved the lower alveolus from right lower canine to left lower molars with ulceration of overlying mucosa. Due to massive size of the swelling, patient was on liquid diet for many years. There was no palpable neck node.

Pre-operative punch biopsy report was revealed as Ameloblastoma. CT scan showed a large expansile lytic lesion involving left hemimandible, with extension to midline region. FOM was indented by the mandibular lesion and caudally there was thickening of left lower GBS—suggestive of neoplastic lesion.

Patient was taken for surgery under General Anaesthesia with nasal intubation on 07/08/2014 and whole of the tumour along with the anterior arch and entire hemimandible on left side and soft tissue from floor of mouth was excised. Reconstruction was done by titanium plate. Post-operative HPE report revealed mesenchymal and epithelial differentiation with the mesenchymal component displaying storiform and herring bone pattern in a fibromyxoid stroma, while the epithelial component was composed of focal ameloblastic islands made up of columnar cells arranged in a palisaded pattern with a central area of stellate reticulum-like cells. Focal areas of necrosis and mitotic figures were seen. These features were suggestive of Ameloblastic fibrosarcoma. Cut margins were found to be free. Patient then underwent Radiotherapy (54Gy in 27#). He is now on regular follow up and doing well

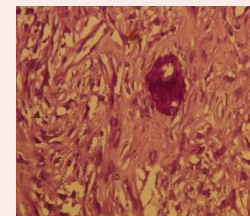
Discussion –

Ameloblastic fibrosarcoma (AFS) was first described by Heath in 1887. It is a rare malignant odontogenic mesenchymal tumour, its epidemiological features still unknown. WHO has defined it as “a neoplasm which has similar structure as ameloblastic fibroma (AF), but in which the mesodermal component shows features of sarcoma.” The most commonly proposed pathogenesis of AFS is transformation of an existing ameloblastic fibroma (AF). Muller et al reported that 44% of AFS had a previous diagnosis of AF. Thus, long term follow-up for recurrences and close monitoring for transformation in addition to complete surgical excision should be done in patients diagnosed as AF.

Ameloblastic Fibrosarcoma always occurs within the jaw bone, with a predilection towards mandible. Clinically, the lesion can cause pain, swelling, paraesthesia and occasionally loss of teeth and ulceration of overlying mucosa. Radiologically, the tumor is like an osteolytic lesion, with ill-defined borders. Histologically, the degree of differentiation is variable, being comparable to a benign fibroma or an anaplastic tumour. Investigations done by Yamamoto et al. showed the presence of keratin in the columnar and polyhedral cells of the epithelial component and vimentin in the ectomesenchymal component verifying the biphasic nature of this tumor. Also, Williams et al., demonstrated alterations of the p53 and c-KIT genes in the sarcomatous component of an anaplastic AFS that transformed from a recurrent AF.

Considering the aggressive behaviour of the tumour and its high tendency to recur, the treatment of choice is radical surgery. Radiotherapy or chemotherapy can be added as an adjuvant to surgery to prevent recurrence or can be given in inoperable case or as a palliative treatment. Prognosis depends on histologic grade, tumor size and adequate surgery with free cut margins.

In conclusion, it can be said that AFS is a rare tumor and long-term follow-up would be required to provide more information on survival and recurrence rates of this tumour.



ROLE OF RE-IRRADIATION IN TREATMENT OF RECURRENT OR SECOND PRIMARY CANCER OF HEAD AND NECK SITE: A REVIEW

Dr Rubu Sunku (Senior Registrar)
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Introduction:

Even today, more than 2/3rd of patients of head and neck cancers will present in advanced stage. Almost half of these patients will have recurrence after radical treatment (1). In Radiation Therapy Oncology Group (RTOG) experience, previously irradiated patient has 1% per year risk of second malignancy (2). Currently, the treatment of choice in these patients is surgery. But very few of them is suitable for curative resection. Next options for such patients are salvage radiotherapy, chemoradiotherapy or palliative treatment. Addition of post op radiation to salvage surgery remains controversial.

Re-irradiation in same site for a recurrent or second malignancy is traditionally considered unsafe and toxic (1). Chemotherapy alone in this setting gives median survival of only 5 to 9 months (3). Therefore, if disease is not resectable, definite re-irradiation with chemotherapy is offered. Even if chance of cancer cure is low, it has to be weighed against the risk of toxicity because there are no other treatment options available.

Prognostic factors of recurrent or secondary head and neck cancer:

Patient's selection and individualisation of treatment is very important in management of recurrent head and neck cancer. Although patient's performance status, age, tumor bulk and many other disease and treatment related factors has to be kept in mind, but the most important factor which influence response to re-irradiation is interval since previous radiation. Longer the duration from previous radiation, lesser chance of developing severe toxicity and higher chance of response to re-irradiation (5). Minimum of 6 months interval from previous radiation is taken as inclusion criteria for re-irradiation by most of the authors (6). In RTOG 9610, patients who had gap interval of more than 3 years between two sessions of radiation had 1 yr survival of 48% compared to 35% survival for those whose interval was less than 3 years (11).

Severe toxicity to previous radiation can be a major contraindication to re-irradiation. Thorough evaluation to assess for pre-existing sequelae of previous radiation should be done before deciding for re-irradiation. Occurrence of osteoradionecrosis is a contraindication for radiation. Re-irradiation is ruled out in presence of cartilage necrosis and edema of arytenoids, which places patient in high risk of aspiration and airway closure (5). Radiation myelitis is another limiting toxicity, which is a contraindication for radiation of any organ in the vicinity of spinal cord. Using

conventional fractionation, the estimated risk of myelopathy is <1% and <10% at 54 Gy and 61 Gy, respectively (21). Carotid blowout is a rare but fatal complication due to re-irradiation. In patients treated in a continuous course with 1.8–2-Gy daily fractions or 1.2-Gy twice daily fractions, rate of carotid blowout was 1.3% (22).

De Crevoisier et al, in the study on role of re-irradiation, found that the only two factors affecting the risk of death is surface and volume of second radiation field. Patients irradiated with an area less than 125 cm² or a volume less than 650 cm³ had higher overall survival rate than that of patients treated with an area more than 125 cm² and a volume more than 650 cm³ (6). This findings were confirmed by Chen et al, in his study where the subset of patients with tumor volume <27 cm³, the 2-year local control rate was 80% (5,8).

Some studies showed that second primary tumor has better prognosis than recurrent disease. This can be explained by presence of resistant clonogen in recurrent case which has survived previous radiation and proliferated over the time (1).

A normogram to assess the prognosis of these patients were developed by Tanvetyanon T et al. This includes performance status, co-morbidity, tumor bulk, isolated neck recurrence and predicts the probability of death within 24 months of re-irradiation.

Treatment Recommendations :

Current management of recurrent head and neck cancer is dependent on its respectability. Surgery is the first choice of treatment in resectable cases. Complete resection gives long term survival of 25% to 45% in these patients. However even after complete resection with negative margins, these patients have risk of local failure of upto 59%(10). Janot et al, on his randomised phase III study on 130 patients showed that adjuvant radiotherapy improved disease free survival when compared with patients who were kept in observation arm, but there was no significant improvement in overall survival (12).

Role of definitive re-irradiation was evaluated by two prospective randomized trials. RTOG trial 9610 and RTOG 9911 demonstrated 2-year survival rates of 15.2% and 25.9%, respectively. However, many questions remain unanswered regarding the optimal delivery of Re-RT and the best Chemotherapy agents, as well as questions regarding selection criteria of patient in order to achieve maximum benefit from radiotherapy or chemoradiotherapy.

Inclusion of lymph nodal region at risk in radiation field, still remain inconclusive. In most of the studies, radiation field included only gross tumor volume with margin for clinical target volume. The margin given to GTV depends on radiotherapy technique employed, either 3DCRT, IMRT or IGRT. Margin varied from 0.5 cm to 2 cm to obtain CTV (6,11,12,14). In some studies CTV margin was reduced to as low as 5 mm when critical organ such as spinal cord and brain stem came in vicinity (15).

Dose prescribed in re-irradiation remains controversial. Higher re-irradiation dose are shown to give better response. In study by Salam et al, 3-year overall survival and locoregional control rate of patients who received re-irradiation dose of > 58 Gy was 30% and 56%, as compared to 6% and 33% in patients who received doses of < 58 Gy (16). Some experimental data showed that head and neck can tolerate cumulative dose of upto 130 Gy, and dose of spinal cord should be limited to 50 Gy (8,17). At present recommended dose for re-irradiation in various studies are 60-70 Gy (8).

Newer treatment modality, such as IMRT (Intensity Modulated Radiation Therapy) or IGRT (Image Guided Radiation Therapy), improves precision, therefore improve therapeutic ratio. Lee et al reported that IMRT has offered possibilities for applying re-irradiation more safely with greater local control. They reported a 2-year disease free survival of 52% vs 20% in patients who underwent IMRT and patients who did not (18).

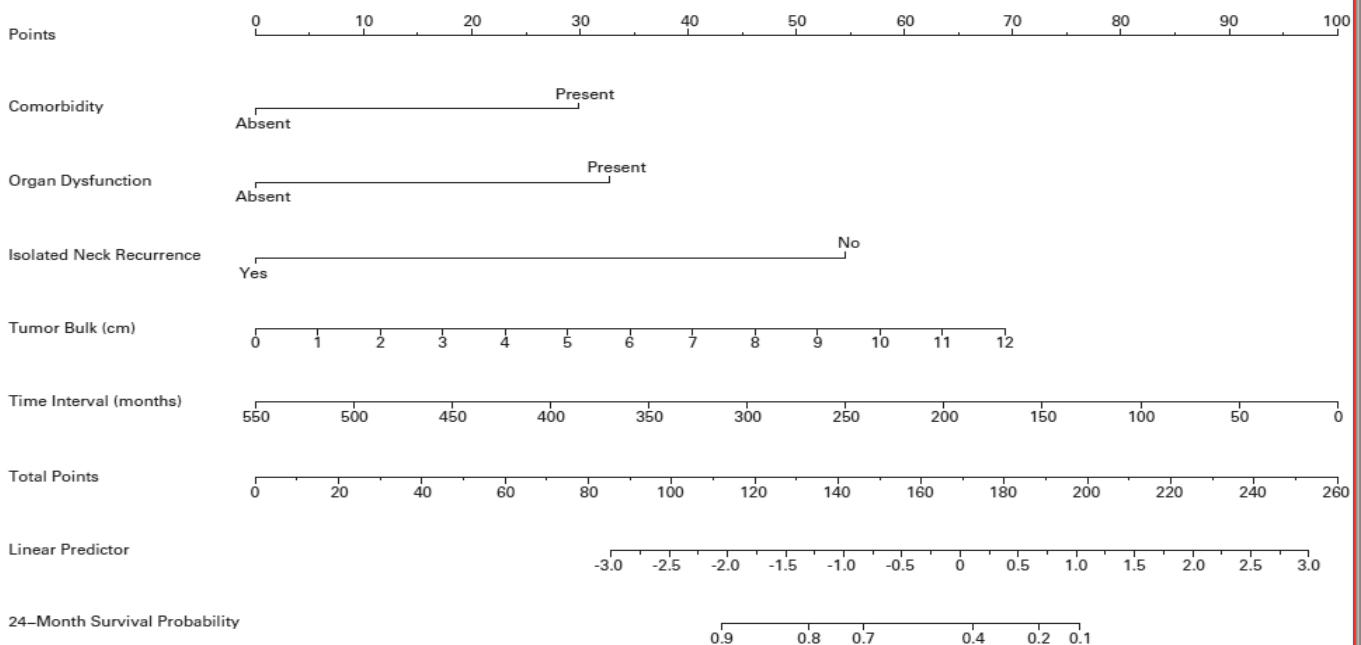
Image guided Radiotherapy improves tumor localization and reduces positioning errors. Stereotactic radiotherapy and radiosurgery is emerging as very good alternative to surgery in recurrent head and neck cancer. Rogh et al reported an 80% response rate after 30 Gy (range 18–40 Gy) in 3–5 fractions administered using the Cyber-Knife system. A 2-year survival rate of 30.9% and a treatment death rate of 2.9% were reported (19). In study by Unger et al, patients

treated with Stereotactic radiosurgery, the 2-year OS and locoregional control (LRC) rates were 41% and 30%, respectively. Higher total dose, surgical resection, and nasopharynx site were significantly associated with improved locoregional control. Surgical resection and nonsquamous histology were associated with improved OS (20).

Conclusion:

Significant number of patients treated for advanced head and neck cancer presents with recurrence. In these patients who presents with inoperable recurrence or second primary, re-irradiation remains the only option. Toxicity due to cumulative dose is an important factor to be kept in mind. Duration of gap between two sessions of radiation, volume of re-irradiated tissues, radiation dosage and use of IMRT/IGRT/SBRT, are some of the factors which determine prognosis of patients with recurrent disease. Therefore, re-irradiation with or without chemotherapy should be administered in well selected patient, to improve locoregional control and progression free survival.

To read the Normogram (figure), obtain the value of each variable and draw a straight line up until this intersects the line labeled as “points”. That value at the point of intersection denotes the number of points incurred. By repeating this process for each factor, a point’s score for each variable is obtained and accumulated. Finally, locate the value of the total points on the horizontal line labeled as “total points” and draw a straight line down, the estimated probability of survival at 24 months is indicated, ranging from 0 to 1.0



Radiation therapy has evolved over the last 2 decades in terms of technique, planning, delivery and also changing radiobiological concepts of tumor. Although the other changes are mostly attributed to the evolution of technology the Radiobiology of the tumor is more of a clinical approach which changes the total dose, fractionation schedule, dose per fraction and overall treatment time of radiotherapy. Responses are described by a model in which the sensitivity (measured by the degree of tissue damage for normal tissues, and tumour recurrence rates for malignant tumours) to fraction size is represented by the ratio of two constants α and β . The lower the ratio of α to β (expressed in Gy), the greater the effect on normal and malignant tissues of changes in fraction size. Healthy tissues of the breast and ribcage are sensitive to fraction size, with α/β values 5 Gy or less compared to squamous cell carcinoma in Head & Neck sites where α/β value for tumour is 10 Gy, so they respond better with hyperfractionation, so small changes in fraction size can produce relatively large changes in the effects of radiotherapy on these tissues. Conventionally breast cancer treatment used to be of 25-31 fractions over a period of 5-6 weeks (Including tumour Bed Boost), but with the radiobiological concept of acute and late reacting tissue and α/β value the Radiation Oncologist tried the new fractionation schedule of Hypo - fractionation in breast External Beam Radiotherapy. Two largest randomised trials from UK were initiated for the same purpose. The START A and START B trial compared different fractionation schedules with the conventional 50 Gy in 25 # over 5 weeks in Breast cancer patient. The long term 10 year follow up data of the patients is now available (Joanne S Haviland et al, *The Lancet*, 2013), and it clearly showed that the new hypo fractionation

schedules were equal in terms of local control rates as shown in tables 1& 2 below. Also the late side effects or the cosmetic effects which were of more concerns were also less or comparable in hypo fractionation schedules. But even though the above factors in both the groups were comparable the major advantage is decreased duration of overall treatment time. In a country like India where there is limited number of Radiotherapy facilities with long waiting list, this could increase the number of patients that can be started treatment earlier compared to previous long conventional schedules. Since the trial included both the BCT and Mastectomy patients it can be applied to all the patients who needs adjuvant radiotherapy to breast or chest wall.

The other most important change is adjuvant radiotherapy indication in post mastectomy patients. The previous consensus was T3 or T4 tumors, 4 or more axillary lymph nodes or patients who had received upfront NACT. Now a days with newer data availability, this concept has been updated with new guidelines from Cambridge University (Mukesh B Mukesh et al, *Radiotherapy & Oncology*; 2014) (Table 3). The high risk and intermediate risk group (with score 3 or more) were given adjuvant RT while low risk (score <3) were observed. The locoregional relapse were comparable in all the three groups at 5 yr (Table 4).

So overall these new evidence based updates will definitely remove the dilemma among the oncologist in referring patients for adjuvant RT. Brachytherapy is also a form of hypo fractionated RT and its role and selection criteria is different but it's a good modality whenever the facility is available.

Table 1 START A Trial				
Total dose / dose per #	No. of fractions	Treatment Duration	LRR at 10 yrs	95% CI
50 Gy/ 2 Gy	25	5 weeks Daily Rx	7.4%	5.5-10.0
41.6 Gy/ 3.2 Gy	13	5 weeks (5 # in fortnight)	6.3%	4.7-8.5
39 Gy/ 3 Gy	13	5 weeks (5 # in fortnight)	8.8%	6.7-11.4

Table 2 START B Trial				
Total dose / dose per #	No. of fractions	Treatment Duration	LRR at 10 yrs	95% CI
50 Gy/ 2 Gy	25	5 weeks Daily Rx	5.5%	(95%CI 4.2-7.2)
40 Gy/ 2.67 Gy	15	3 Weeks Daily Rx	4.3%	(95%CI 3.2-5.9)

Table 3 Cambridge Post Mastectomy Radiotherapy Index (C - PMRT)			
Score	3	2	1
Number of positive lymph nodes or LVI	≥4	1-3	LVI
Invasive tumour size	>50 mm (T3) or T4	30-50mm	20-29mm
Excision margins	Deep margin < 1mm or muscle invasion	-	-
Tumour grade	-	-	Grade 3

Table 4	LRR (%)	Risk group	Isolated LRR (%)	Risk group
Chest wall	22 (52.4%)	H: 10, I: 3 and L: 9	9 (64.3%)	H: 1 and L: 8
Axilla LN	11 (26.2%)	H: 9 and L: 2	4 (28.6%)	H: 2 and L: 2
SCF LN	5 (11.9%)	H: 2 and I: 3	1 (7.1%)	H: 1
IMC LN	1 (2.4%)	I: 1	0	-
Chest wall + regional nodes	3 (7.1%)	H: 3	0	-
Total patients	42		14	

LN: lymph nodes.
IMC: internal mammary chain.
H: high risk group.
I: intermediate risk group.
L: low risk group.

C - PMRT- LRR in three groups

AONEI : EVENTS AND ACTIVITIES



Run for Breast Cancer, Guwahati



Mayang Cancer Awareness Camp



Nalbari Cancer Awareness Camp



Diphu Cancer Awareness Camp





Exchange of Scientific Knowledge



Improvement of The Standard of Oncology Practice in North East



Collaborative Work



Organisation of Periodical Conference, Continuing Medical Education Programmes, Symposia, Workshops in Different Parts of The Region



Publication of Scientific Writing



Social and Community Work

AIMS

AONEI COMMITTEE

- ❖ Adviser: Dr. P K Choudhary
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- ❖ Secretary: Dr. J N Buragohain
- ❖ Vice President: Dr. K Ahmed
- ❖ Asst. Secretary: Dr. A K Kalita
- ❖ Treasurer: Dr. A K das
- ❖ Editor: Dr. Vikas Jagtap

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- Dr. Shyam Tsering (Arunachal Pradesh)
- Dr. Jeremy L Pautu (Mizoram)
- Dr. Ashish Rai (Sikkim)

UPCOMING EVENT

Annual AONEI Conference
Hotel Rendezvous : 4th and 5th April 2015.
 Gangtok (Sikkim)
 Organizing Secretary: Dr. Ashish Rai
asoorai@gmail.com, +919593387501

Lymphoma Updates
 September 2015
 Guwahati
 Organised by: Department of Medical Oncology
 Dr. B Borooah Cancer Institute, Guwahati-16

NE – AROI Zonal Chapter Annual Conference
 2nd & 3rd October
 Guwahati
 Organizing Secretary: Dr. Vikas Jagtap
drvikasi@yahoo.co.in, +918822231236

CANCER TREATMENT FACILITIES IN NORTH EAST INDIA

- ❖ Dr. B Borooah Cancer Institute, Guwahati, Assam
- ❖ North East Cancer Hospital & Research Institute, Guwahati, Assam
- ❖ Cachar Cancer Hospital & Research centre, Silchar, Assam
- ❖ SMCH, Silchar, Assam
- ❖ Assam Medical College & Hospital, Dibrugarh, Assam
- ❖ Civil Hospital, Shillong, Meghalaya
- ❖ NEIGRIHMS, Shillong, Meghalaya
- ❖ RIMS, Imphal, Manipur
- ❖ Aizawl Civil hospital, Aizawl, Mizoram
- ❖ Naharlagun General Hospital, Itanagar, Arunachal Pradesh
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- ❖ STNM Hospital, Gangtok, Sikkim