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Original Article

Dosimetric Comparison Between Cone and Micro Multi Leaf Collimator-Based Stereotactic Radio Surgery Plans for Brain Metastases

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ABSTRACT

Background: Brain metastases are the most frequent type of neurological complication of cancer and portend significant morbidity and mortality. Treatment options include conventional surgery, whole-brain radiation therapy (WBRT), stereotactic radiosurgery (SRS), and systemic therapies. For those patients eligible for SRS, it is a highly precise treatment modality. This study aimed to compare dosimetric parameters between cone-based and micro-multileaf collimator (mMLC)-based stereotactic radiosurgery plans for brain metastases and to identify appropriate clinical scenarios for each technique.

Methods: A total of 28 patients aged more than 18yrs with 36 metastatic lesions in the brain, fulfilling inclusion criteria were selected in our study after obtaining ethical committee clearance and were recruited for two years from September 2018 to October 2020 and treatment was delivered based on the most optimum plan. Both plans were generated for each patient on the Monaco treatment planning system (version 5.51.10) and were compared concerning target coverage, dose fall off beyond target and doses to the organ at risk. The treatment system included mMLC or Cones of variable sizes as an add-on device on Elekta versa HD linac. The data was tabulated in an MS excel sheet. Statistical analysis was performed using non-parametric small sample t-test, mean was obtained for both Cones and mMLC, p-value <0.05 was considered statistically significant.

Results: The mean of conformity index for mMLC was 1.11+0.12, the cone was 1.06+0.11 and p value was 0.206 which is statistically insignificant. The homogeneity index for mMLC was 1.15 +0.13, the Cone was 2.43+1.86, the gradient index for mMLC was 5.37 + 2.73, the Cone was 3.06 + 0.76, the quality of coverage for mMLC was 0.91 +0.11, the Cone was 0.53+ 0.21, the MU for mMLC was 3355.35 + 1665.37, the Cone was 5822.53 + 3051.96 and V12Gy to the brain in mMLC was 8.14 + 5.53, the Cone was 2.70 + 2.02. were statistically significant respectively.

Conclusion: For solitary targets <2cm, regularly shaped, conformal plan with better sparing of normal brain tissue and surrounding OARs could be achieved with Cones than with mMLCplans.For solitary targets between 2 and 2.5 cm, regularly shaped, both the plans are comparable with respect to conformity and MUs. As homogeneity favours, mMLC plans and dose fall off and normal brain tissue sparing favours Cones, both the plans are acceptable as all these parameters are within normal limits.For solitary targets, more than 2.5 cm, irrespective of the shape, better conformity, homogeneity and adequate sparing of normal brain tissue is achievable with mMLC.For multiple lesions, Cones achieve good conformity, homogeneity and better dose fall off and hence better sparing of normal tissue compared to mMLC. Hence Cones are preferred to mMLC in multiple small regularly shaped targets. Therefore for small, spherical or elliptical targets Cone-based plans show dosimetric superiority over mMLC. For large and irregular targets, mMLC is advantageous compared to Cones.

***Keywords**: Brain Metastases; Stereotactic Radiosurgery (SRS); Micro-Multileaf Collimator (mMLC); Cone-Based Radiosurgery; Dosimetric Comparison.*

INTRODUCTION

Brain metastases are the most common neurological complication of cancer, occurring in nearly 30% of patients with malignancies and are associated with poor clinical outcomes. Among all primary cancers, lung cancer is the leading source of brain metastases, accounting for approximately 50% of cases, followed by breast cancer, which contributes 15-20%, as reported by Suh JH et al [1].

Patients with brain metastases often require prompt symptom control to alleviate neurological deficits and preserve quality of life. Supportive management includes corticosteroids to reduce peritumoral edema and anticonvulsants for patients with seizures or those at risk. Definitive treatment options comprise surgical resection, whole-brain radiotherapy (WBRT), and stereotactic radiosurgery (SRS). According to Paul Okunieff et al., the choice of treatment is guided by several factors, including the patient's prognostic status, primary tumor histology, and the size, location, and number of brain metastases [2].

Stereotactic radiosurgery (SRS), either as a standalone treatment or as a boost to whole-brain radiotherapy, is an effective non-invasive treatment option for patients with a limited intracranial metastatic burden. It has become one of the cornerstone treatment modalities for brain metastases. According to Paul Okunieff et al., SRS is particularly indicated for patients who are medically inoperable or for those with lesions that are not amenable to surgical resection because of their location or the number of metastases [2].

SRS is a highly conformal radiotherapy technique that delivers a single fraction of high-dose radiation with submillimeter precision to well-defined, small intracranial lesions while minimizing the dose to surrounding normal brain tissue. It can be delivered using a Gamma Knife, linear accelerator (LINAC), or particle accelerator-based system. Traditionally, SRS was performed using invasive stereotactic head frames for patient immobilization. However, advances in image guidance and immobilization techniques have enabled frameless SRS using non-invasive immobilization devices, offering comparable treatment accuracy with improved patient comfort and convenience.

This study has been chosen for the optimum selection of patients for either technology in terms of target coverage and dose to the organs at risk.

MATERIALS AND METHODS

This prospective study was conducted at Kidwai Memorial Institute of Oncology, Bengaluru, between September 2018 and October 2020 after obtaining approval from the institutional ethics committee. A total of 28 patients with 36 brain metastases were selected. CT simulation (Philips brilliance CT big bore) was done with the patient in the supine position, immobilized with a thermoplastic head mask; fiducial marks were placed. IV contrast of 1ml/kg body weight was given. Scans of 1-2mm thickness were obtained.

Images were transferred to the treatment planning system and fused with diagnostic MRI (T1w). The target volume was the enhancing metastatic lesion with a 1mm margin. Organs at risk were contoured. Treatment plans were done on the Monaco treatment planning system (version 5.51.10)

1 Cone and 1 mMLC-based plan were generated for each patient. For Cone-based planning, a circular collimator of varying sizes between 2.5mm and 15mm was used depending on the lesion size. Multiple cones were used when the lesion size exceeded the maximum available cone diameter. For mMLC-based planning, MLC having 56 leaf pairs, with a leaf width of 2.5mm at the isocentre, was used.

Dose to the target was decided based on the maximum diameter of the lesion.4
If the lesion is <2cm 21 to 24 Gy
2-3cm 18Gy
3-4cm 15Gy

Doses were prescribed to the isodose covering the target, with a minimum of 60% isodose line for Cones and 80% isodose line for mMLC plans.

Two plans were compared concerning the conformity index, homogeneity index, gradient index, quality of coverage and doses to the organs at risk. The data were tabulated in an MS excel sheet. Statistical analysis was done using a nonparametric small sample t-test in the statistical package for the social sciences (SPSS) software version 28. The Mean was calculated after tabulating the values, and the standard deviation (SD) was obtained for each variable. P value was calculated, and p-value <0.05 was considered significant.

RESULTS

The overall mean of conformity index for mMLC was 1.11±0.12, the Cone was 1.06±0.11 and p value was 0.206 which is statistically insignificant.

The mean of homogeneity index for mMLC was 1.15 ±0.13, the Cone was 2.43±1.86 and p value 0.01. The mean of gradient index for mMLC was 5.37 ±2.73; the Cone was 3.06 ± 0.76, p value 0.001.The mean of quality of coverage for mMLC was 0.91 ±0.11, the Cone was 0.53 ± 0.21, p value 0.01. The mean of MU for mMLC was 3355.35 ± 1665.37, the Cone was 5822.53 ± 3051.96 When V12Gy to the brain was compared between mMLC and cone it was found that mean V12Gy for mMLC was 8.14 ± 5.53, the Cone was 2.70 ± 2.02. p value 0.001 (statistically significant).

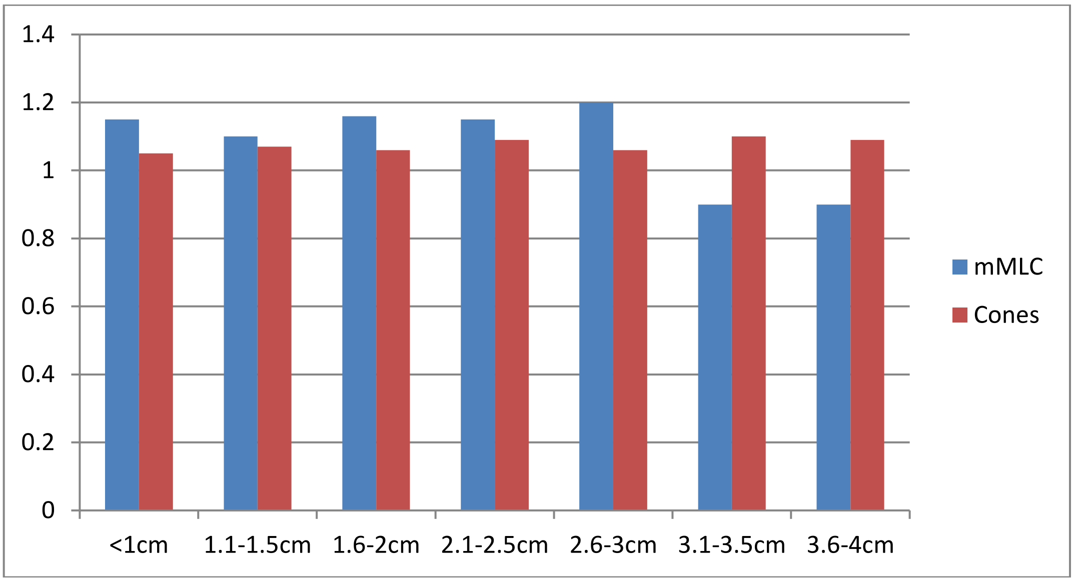


Figure 1

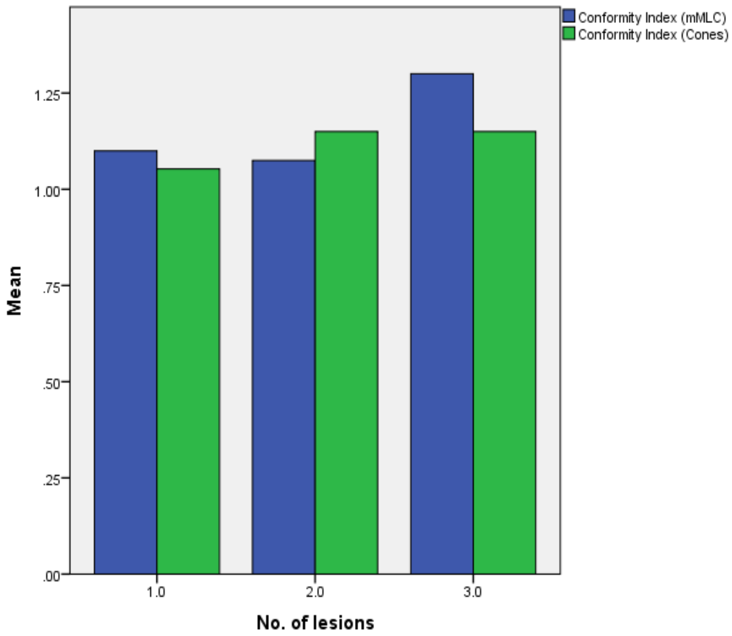


Figure 2

Figure number 1 and 2 shows the Conformity Index between mMLC and Cones

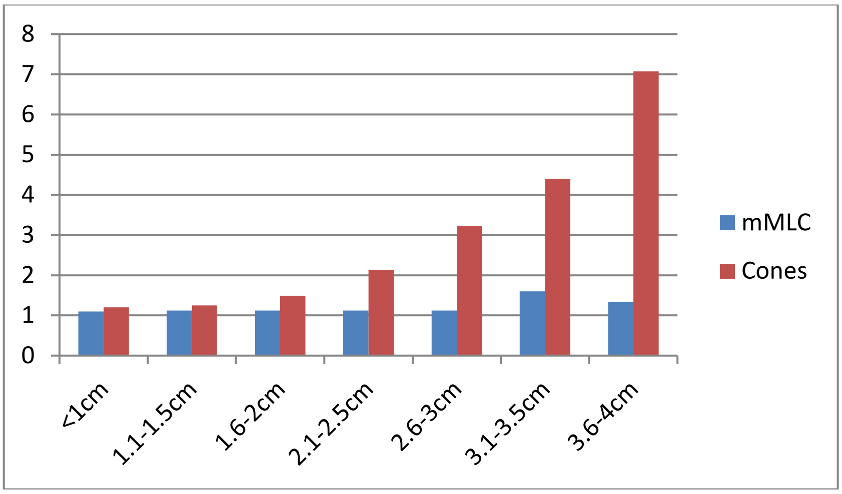


Figure 3

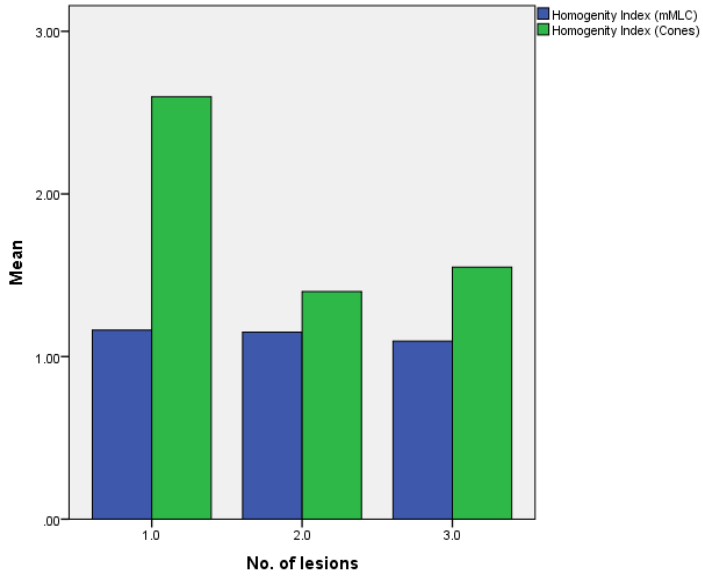


Figure 4

Figure no 3 and 4 shows the Homogeneity Index between mMLC and Cones.

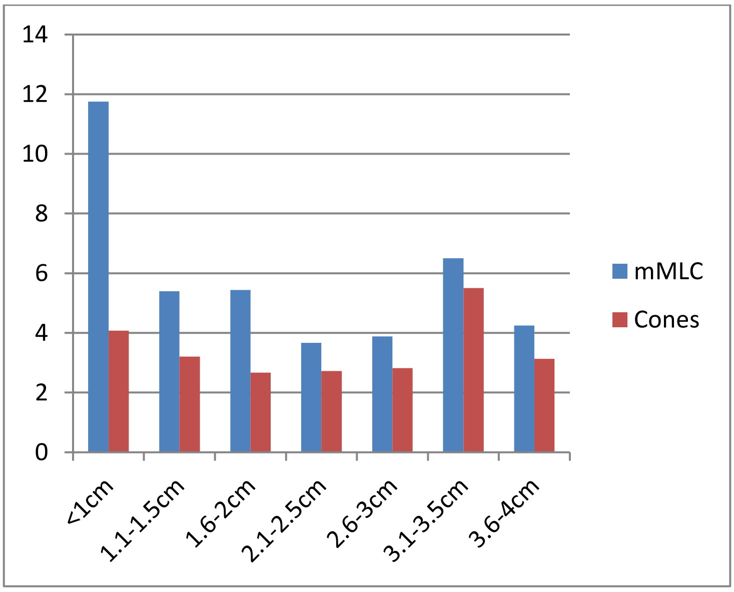


Figure 5

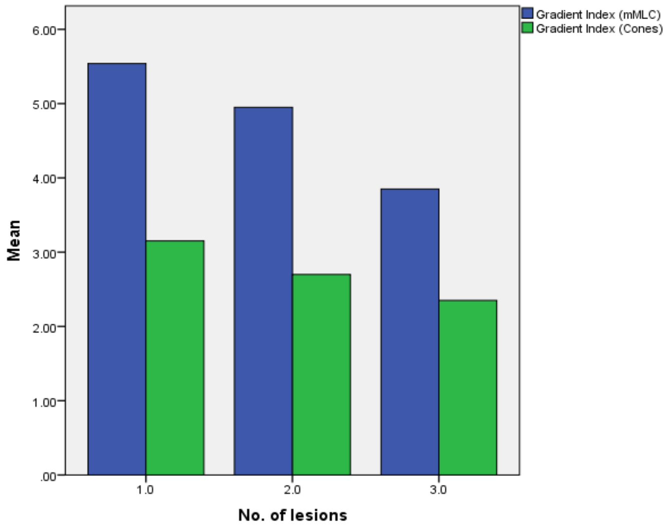


Figure 6

Figure no 5 and 6 shows the Gradient Index between mMLC and Cones.

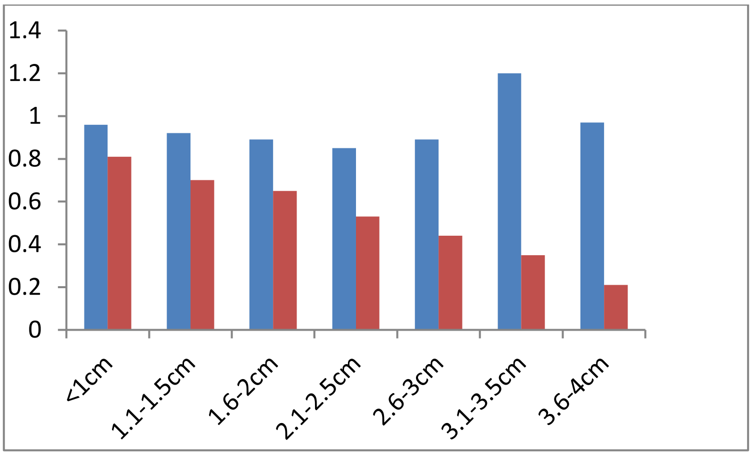


Figure 7

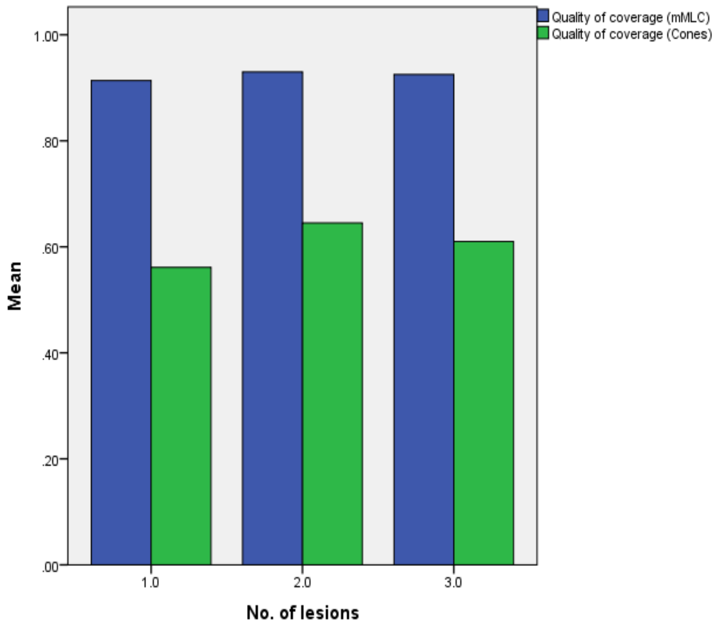
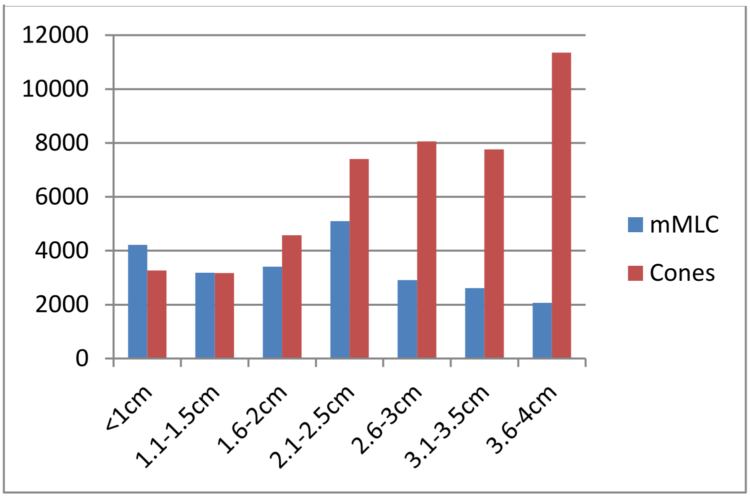


Figure 8

Figure no 7 and 8shows the Quality of coverage between mMLC and Cones.

Figure 9



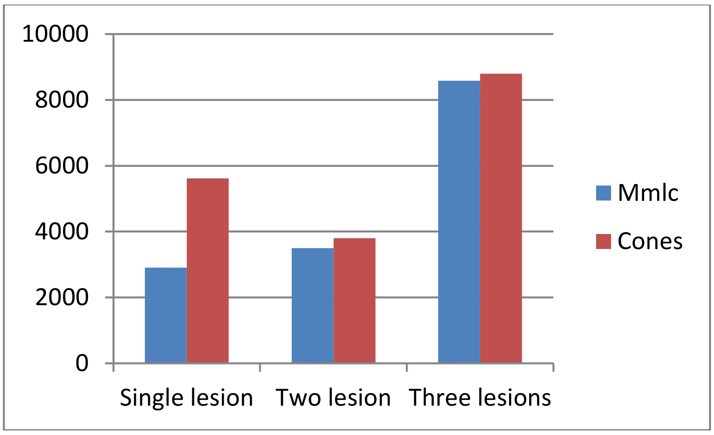


Figure 10

Figure no 9 and 10 shows the Monitor units between mMLC and the cones

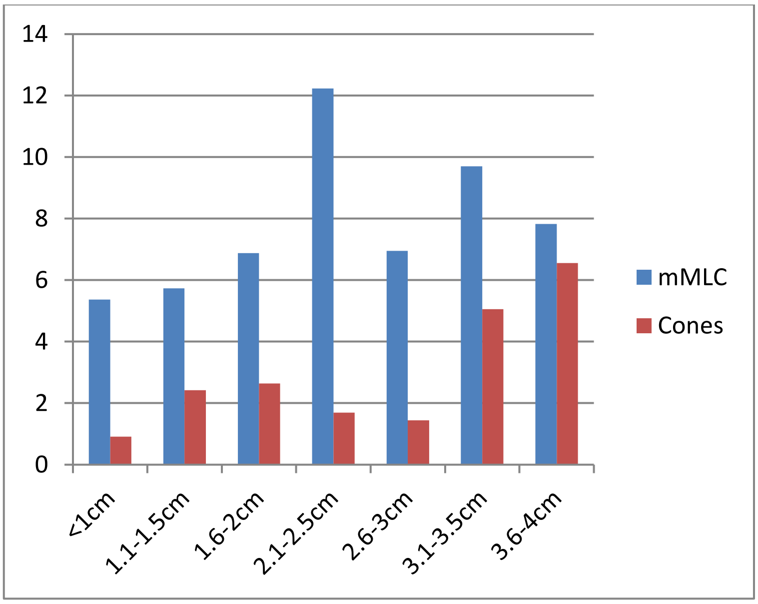


Figure 11

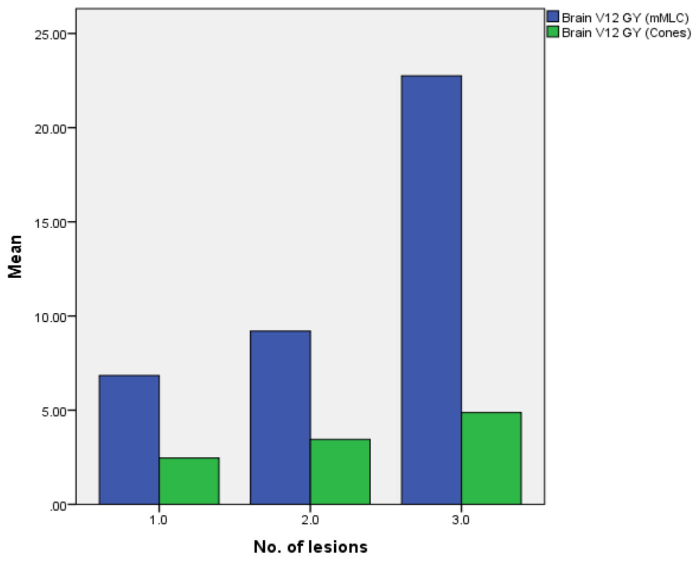


Figure 12

Figure 11 and 12 shows 12gy receiving volume of the brain

DISCUSSION

The brain is a frequent site of metastatic spread, with approximately one-third of patients with cancer developing brain metastases, which represent the most common neurological complication of systemic malignancy. Such patients need immediate control of symptoms with anti-oedema and anticonvulsant drugs, and specific management includes surgery, whole brain RT and stereotactic radiosurgery. Prognostic factors, histology, size and the number of metastatic lesions will decide the treatment modality.

Of those patients eligible for radiosurgery, a comparison was made between Cone and mMLC based plans, which would help in delivering appropriate treatment for patients planned for radiosurgery at our institution

Prescription isodose (PI) varied from 80 to 100 percent for mMLC and 60 to 100 percent for cones which is contrary to the study by Y J Si et al [3], where the prescription isodose was set to 80 percent for both cone and MLC-based plans as the maximum dose between the two plans were not compared in their study.

The target's maximum dose (%) was compared between mMLC and Cones. The Maximum dose in all mMLC plans didn't exceed 150%, whereas in cone-based plans for lesions above 2.5 cm, max dose exceeded 200%, which is unacceptably high. This occurred due to the overlapping spherical isodose of multiple isocentres used to avoid cold spots within the target. This was similar to the study by Salim et al [4], where gamma knife plans were compared with VMAT plans in pituitary adenomas and vestibular schwannoma in which the hot spot was limited to 200%.

In our study, the Conformity index (CI) was lower in Cone-based plans than in mMLC plans (mean CI mMLC 1.11, cones 1.06), but it was not statistically significant (p-value 0.206), which is as per RTOG quality assurance guidelines for radiosurgery developed by Shaw E et al [5] . During slice-by-slice plan quality evaluation, it was observed that all lesions more than 2.5 cm in Cone-based plans had under coverage in the peripheral slices of the target; in contrast, the same wasn't observed in mMLC plans. Also, when the target is asymmetrical, the dose was well conformed to the target in mMLC than with Cone plans. This is explained in the study conducted by Y Cedric et al [6], where multiple beam arcs controlled by different sizes of cones produce spherical or elliptical dose distribution, which reduces the conformity of irregularly shaped targets . This shows that this parameter lacks spatial information; hence slice-by-slice plan evaluation is critical in making decisions. This was similar to the Study by Y J Si et al [3] where they compared CI for cone-based and MLC-based cyber knife SRS plans; CI was lower in cone based than in MLC-based plans (median CI for mMLC 1.3, cones 1.2), indicating better conformity of Cone based plans.

All mMLC plans, irrespective of the size and number of lesions, had Homogeneity Index(HI) less than 2, which is as per RTOG quality assurance guidelines for radiosurgery developed by Shaw E et al [5] .Whereas in cone plans homogeneity index was less than 2 in lesions less than 2cm, Lesions between 2 and 3 cm had HI between 2 and 2.5, i.e., with minor deviation as per RTOG but acceptable. Lesions more than 3 cm had HI more than 2, a major deviation as per RTOG protocol. Hence lesions more than 3 cm planned with cones had more heterogenous dose distribution. Therefore mMLC plans are superior concerning HI in more than 3 cm lesions.

The gradient index (GI) can be used to compare treatment plans of equal conformity. The steep dose gradient outside the target makes radiosurgery possible. Therefore it is sensible to measure and use this variable to compare rival plans or treatment modalities. Irrespective of the number of lesions and those lesions more than 1 cm had a gradient index better with cones than with mMLC plans because of the rapid fall of the dose beyond the target with cones, which will reduce the dose received by the surrounding brain tissue and other organs at risk (OAR). (mean GI for cones 3.06 + 0.76, for mMLC 5.37 + 2.73) The overall difference is significant statistically (p-value 0.001). The GI results show that mMLC is the most inferior amongst small target diameters (<1cm) due to inherent dose spillage in these treatments, but it was not statistically significant. When we re-assessed the plans of those lesions less than 1cm, it was found that there were two lesions in that category and the difference in the GI for both lesions in mMLC plans was too high. This may be because a small variation in the lesion size in such small tumors would lead to a large relative change (i.e., GI). This is similar to the study conducted by Duan Y et al [7] where they compared gamma knife, cone VMAT and MLC-based CRT. (mean GI in gamma knife 2.6+0.07, cone 2.66 + 0.16, MLC 5.4+ 1.08) Hence cone-based plans are better concerning GI, especially in lesions less than 1 cm.

As per S Julia et al study [8] quality of coverage(QOC) indicates the minimum dose in the target; when it's closer to the prescription dose, the value will be close to 1. It is used as a complementary to CI. In our study all mMLC plans, irrespective of the size and number of lesions, had a superior quality of coverage compared to Cone plans.

Concerning monitor units, mMLC plans had lesser MUs irrespective of the size and number of lesions being treated. Still, the difference was statistically insignificant, up to 2.5cm in patients with multiple lesions. Therefore in lesions above 2.5cm, mMLC is found to be superior as the lesser the MUs lesser the treatment time, which is comfortable for patients with brain metastases and also for institutions like ours where the patient load is high. Increased modulation, often when more stringent constraints are applied during the optimization process, will result in higher MUs. This was similar to the Study by Vergalasova et al [9] where they compared intracranial SRS plans of gamma knife, elements dynamic conformal arc (DCA), manual and hyperarc VMAT, and showed that the MUs and beam on time were more for gamma knife than DCA and VMAT based plans.

The dose received by the adjacent organs is the most critical safety measure taken to prevent damage to normal tissues. Our study compared the dose received by adjacent organs between mMLC and cones.

All cases, irrespective of size and the number of lesions, had a lesser volume of brain receiving 12Gy with Cones compared to mMLC; thus, with cones, there is much sparing of normal brain tissue. (mean V12Gy for cone 2.70cc, mMLC 8.14cc) This result was similar to the study by Yongsook et al [10] where they compared Circular collimator arc(CCA) with dynamic conformal arc(DCA) treatment plans for linac-based stereotactic radiosurgery of intracranial targets of volume less than 1.4cc (mean V12Gy for CCA 1.37cc, DCA 1.43cc). This was also similar to the study conducted by Vergalasova et al [9], where they compared intracranial SRS plans of gamma knife, elements(DCA), manual and hyperarc VMAT, and showed that the V12Gy to the brain was lower with gamma knife, compared to manual VMAT and DCA plans. Those plans with multiple lesions had V12Gy more than 10cc in mMLC plans. Hence cones are preferred in such cases as the risk of symptomatic radio necrosis rapidly increases when the volume of the brain receiving 12Gy is greater than 10cc, which is evident from the study conducted by Giuseppe et al [11].

Although other OARs received doses lesser with Cone based plans than with mMLC plans, dose constraints were met in both plans. Dose constraints for other OARs were adopted from the study by T Micheal et al [12].
Plan evaluation is mainly by three-dimensional visualization of isodose distribution; all these above-studied parameters are complementary to section-by-section plan assessment.

CONCLUSION

For solitary targets <2cm, regularly shaped, conformal plan with better sparing of normal brain tissue and surrounding OARs could be achieved with Cones than with mMLC plans.

Both plans are acceptable for a solitary target between 2 and 2.5 cm, regularly shaped, as all the comparison parameters are within normal limits. Hence it is left to the discretion of the treating physician to choose the treatment modality for this kind of targets

For a solitary target of more than 2.5 cm, irrespective of the shape, better conformity, homogeneity and adequate sparing of normal brain tissue is achievable with mMLC.

For multiple lesions, cones achieve good conformity, homogeneity and better dose fall off and hence better sparing of normal tissue compared to mMLC, hence cones are preferred to mMLC in multiple small (less than 2 cm) regularly shaped targets.

Therefore, for small, spherical or elliptical targets cone-based plans show dosimetric superiority over mMLC. For large and irregular targets, mMLC is advantageous compared to Cones

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