Quantifying Systematic Bias In Caliper-Based Tumor Volume Measurements Using Micro-CT

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ABSTRACT

Purpose:
Murine models of head and neck squamous cell carcinoma (HNSCC) are routinely monitored using external caliper measurements to estimate tumor volume, most often relying on simplified geometric assumptions such as cylindrical approximations. While convenient, these approximations do not reflect the heterogenous morphology and tumor shape. Therefore, in this study, we directly compared caliper-derived tumor volumes with day-matched volumetric measurements obtained from micro–computed tomography (μCT).

Methods:
117 mice were inducted into the right buccal mucosa with either Moc1(n=42), MLM1(n=39) and Moc2(n=36) tumor cells. Once tumors reached approximately 50mm^3 they were treated with 2 fractions of 8Gy radiation with 5mg/kg cisplatin with one weeks apart. 7 days post treatment mice underwent micro-PET/CT imaging to assess tumor volume, and caliper measurements were taken the same day. Tumor volumes from caliper measurements were calculated using a cylindrical approximation. Tumor volumes from micro-PET/CT were calculated by contouring the volume in three dimensions via a Hounsfield thresholding with values ranging from 75-300HU. Volumes derived from CT were considered ground truth as they were able to encompass the irregular shape.

Results:
Linear regression analysis demonstrated a strong but non-unity relationship between the two measurement approaches, with a fitted slope of 0.72, indicating that caliper-based methods systematically underestimate tumor volume relative to CT-derived measurements. This consistent bias enables applying a systematic correction factor to improve the accuracy of caliper-derived tumor volume estimates.

Conclusion:
This study highlights the limitations in simple geometric approximations and emphasizes the importance of incorporating image based volumetric analysis when precise tumor burden quantification is required such as studies evaluating treatment response.

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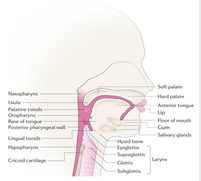
INTRODUCTION

- Head and neck cancer is the 6th most common cancer worldwide [1] with Head and Neck Squamous Cell Carcinoma (HNSCC) accounts for approximately 90% of all head and neck cancers [2]
- Standard treatment: surgery followed by chemoradiation therapy
- Heterogeneous tumor microenvironment and immune response to therapy making it difficult to predict treatment response[1]
- Various studies have shown a strong correlation between tumor volume and treatment response[3,4]
- Tumor volume measurements are often monitored to evaluate treatment effectiveness as well as guide decisions such as when to treat.
- However, tumor volumes are typically limited to external caliper measurements and geometric approximations that cannot capture important tumor features.
- This study aims to understand the systematic bias using caliper-based tumor volume measurements compared to CT rendered measurements



METHODS AND MATERIALS

- 117 mice were orthotopically injected with either MOC1 (N=42) MLM1 (n=39) and MOC2 (n=36) tumor cells.
- When tumors reached ~50mm^3 mice received 2x8Gy radiation with 5mg/kg cisplatin on Day 0 and 7.
- On day 14 mice underwent μPET/CT images while also having an external caliper measurement
- Tumors were contoured using Hounsfield thresholding between 75-300HU and then Gaussian smoothed
- Volume calculation occurred using three methods:
  - External caliper measurement where $V_{tumor} = \frac{\pi}{6} * length * width^2$
  - Cylindrical approximation from CT rendered meshes
  - Volume determined by CT segmentation and voxel counting

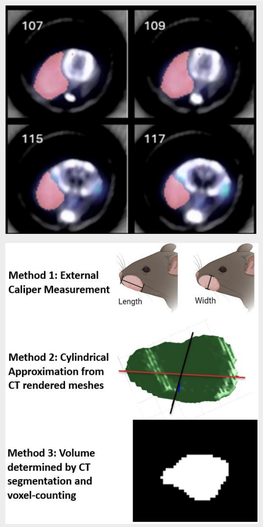


Figure 1 (Top): Example contour of mouse tumor
Figure 2 (Bottom): Various methods used to determine tumor volume. Method 1 used external measurements and the cylindrical approximation. Method 2 applied the cylindrical approximation on CT meshes. Method 3 demonstrates the most accurate measurement by performing CT segmentation and voxel counting

RESULTS

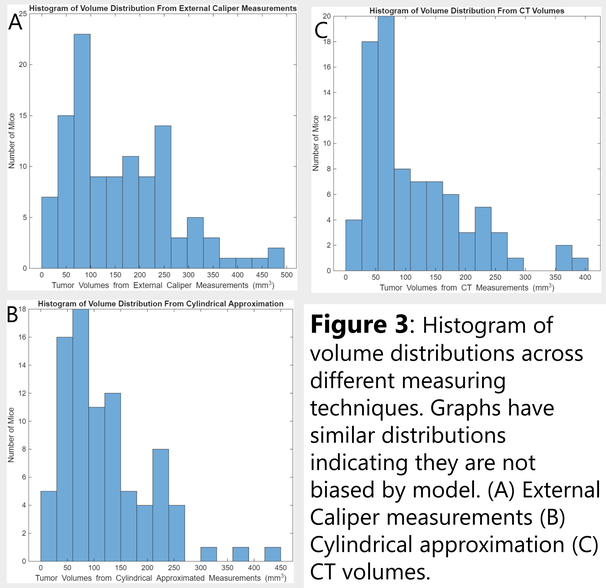


Figure 3: Histogram of volume distributions across different measuring techniques. Graphs have similar distributions indicating they are not biased by model. (A) External Caliper measurements (B) Cylindrical approximation (C) CT volumes.

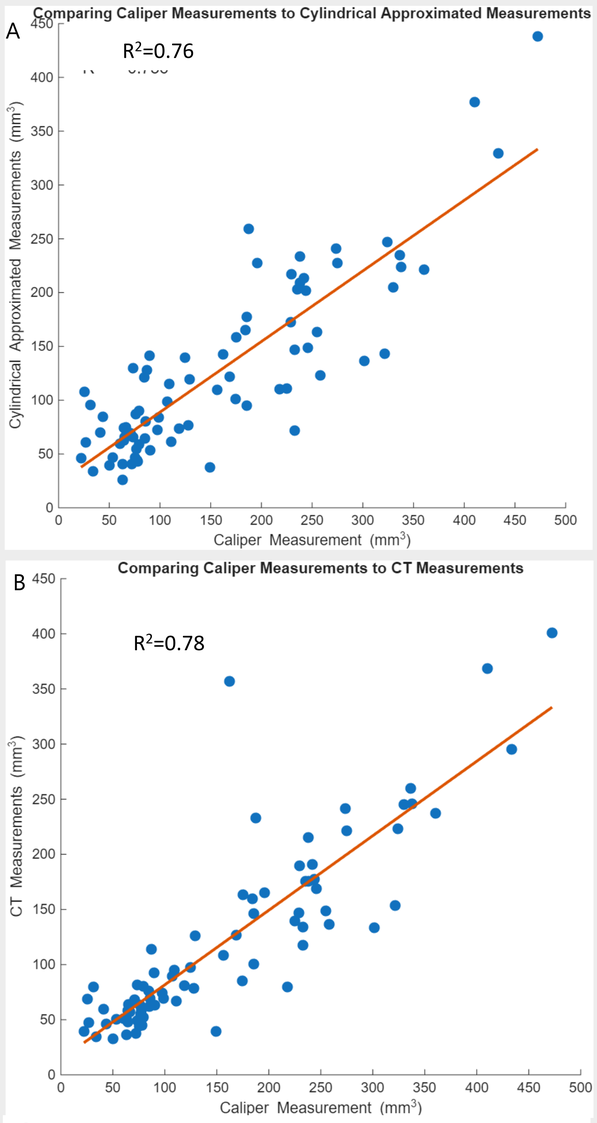


Figure 4: Comparison of caliper measurements to both cylindrical approximated measurements and CT measurements. Caliper measurements were more fit with the CT measurements than the measurements derived from cylindrical approximated meshes. In both cases the caliper measurements overestimated the volume which can be useful in developing a correction factor. (A) Comparing caliper measurements to cylindrical approximated (B) Comparing caliper to CT measurements

RESULTS

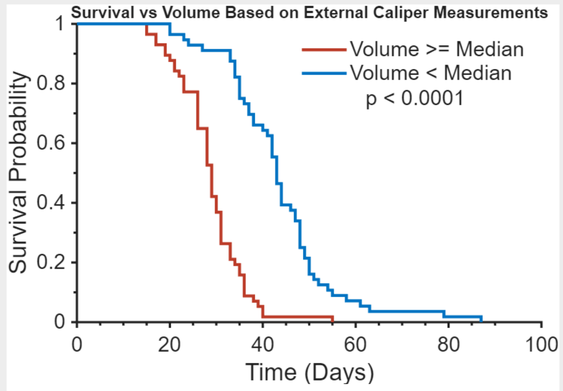


Figure 5: Based on the median volume there was a significant difference in survival from day 14 caliper measurements. This was also applicable to the CT measured volumes.

DISCUSSION

- A large preclinical study was done and investigated the systematic bias in caliper measured volume vs CT rendered volume
- Three tumor models were used with varying growth patterns which eliminated any bias
- There was a systematic overestimation of volume using caliper measurements emphasizing the need for image-based volumetric analyses when precise tumor volume quantification is required

CONCLUSIONS

These findings underscore the importance of incorporating image-based volumetric analysis when precise tumor burden quantification is required, particularly in studies evaluating treatment response, where small volumetric differences can meaningfully influence biological interpretation and experimental conclusions

REFERENCES

1. Johnson, D.E., Burtness, B., Leemans, C.R. *et al.* Head and neck squamous cell carcinoma. *Nat Rev Dis Primers* **6**, 92 (2020). https://doi.org/10.1038/s41572-020-00224-3
2. Cramer, J.D., Burtness, B., Le, Q. *et al.* The changing therapeutic landscape of head and neck cancer. *Nat Rev Clin Oncol* **16**, 669–683 (2019). https://doi.org/10.1038/s41571-019-0227-z
3. Jakovljevic, S., Djordjevic, V., Tomanovic, N. *et al.* The Impact of Primary Tumor Volume on Survival of Patients with Non-Surgically Treated Advanced-Stage Hypopharyngeal Cancer–Retrospective Study and Literature Overview. *Indian J Otolaryngol Head Neck Surg* **77**, 184–193 (2025). https://doi.org/10.1007/s12070-024-05139-z
4. Doweck, I., Denys, D. and Robbins, K.T. (2002), Tumor Volume Predicts Outcome for Advanced Head and Neck Cancer Treated With Targeted Chemoradiotherapy‡‡. The Laryngoscope, 112: 1742-1749. https://doi.org/10.1097/00005537-200210000-00006

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