Metabolic imaging of head and neck cancer organoids

Amy T. Shah,Tiffany M. Heaster

[1]*Department of Biomedical Engineering, Vanderbilt University, Nashville, TN, United States of America*
[2]*Department of Biomedical Engineering, Vanderbilt University, Nashvill*

Abstract (600 words limit)

Head and neck cancer patients suffer from toxicities, morbidities, and mortalities, and these ailments could be minimized through improved therapies. Drug discovery is a long, expensive, and complex process, so optimized assays can improve the success rate of drug candidates. This study applies optical imaging of cell metabolism to three-dimensional in vitro cultures of head and neck cancer grown from primary tumor tissue (organoids). This technique is advantageous because it measures cell metabolism using intrinsic fluorescence from NAD(P)H and FAD on a single cell level for a three-dimensional in vitro model. Head and neck cancer organoids are characterized alone and after treatment with standard therapies, including an antibody therapy, a chemotherapy, and combination therapy. Additionally, organoid cellular heterogeneity is analyzed quantitatively and qualitatively. Gold standard measures of treatment response, including cell proliferation, cell death, and in vivo tumor volume, validate therapeutic efficacy for each treatment group in a parallel study. Results indicate that optical metabolic imaging is sensitive to therapeutic response in Salaries constituted the major component (42.6%) of this cost, followed by equipment/furniture (29%), space rent (20.7%), overheads and consumables (7.7%). In addition, INR 47,191 (USD 773) per HNC patient was spent on the surgery. Furthermore, patients spent an average amount ranging from INR 12,575 (USD 206) to INR 65,257 (USD 1069) on the different treatment therapies. In terms of package rates, cobalt radiotherapy alone was the cheapest (INR 38,714, USD 634), while intensity modulated radiotherapy (IMRT) was most expensive (INR 192,914, USD 3161). The estimates from the present study could be used for developing package rates under various publicly financed health organoids after 1 day of treatment ($p<0.05$) and resolves cell subpopulations with distinct metabolic phenotypes. Ultimately, this platform could provide a sensitive high-throughput assay to streamline the drug discovery process for head and neck cancer. There are no published data on the cost of cancer treatment for guiding reimbursement decisions in India. The present study was designed to estimate the cost of treating head and neck cancer (HNC) with the aim of determining package rates. The present study was undertaken in the Departments of Radiotherapy and Otolaryngology of a large tertiary care hospital in North India. Economic health system costs incurred were assessed using a bottom-up methodology. Data on all resources–capital or recurrent, incurred on the delivery of HNC treatment were collected from April 2014 to March 2015. Following the cost-of-illness approach, patients were interviewed to elicit out-of-pocket (OOP) expenditure. A total of INR 40,993,017 (USD 0.67 million) was spent on radiotherapy care for treating HNC during 1 year.

insurance schemes as well as for the planning for creation of new cancer centresThe budget allocation towards cancer-specific spending in India has increased from INR 115 million in the sixth plan (1980–1985) to INR 28,719 million and INR 60,000 million in eleventh and twelfth five-year plan, respectively. Furthermore, since 2007, a large amount of money has been pooled towards cancer care by the Government of India through various publicly sponsored health insurance schemes. Also, certain states such as Punjab provide cashless cancer treatment in various public and private sector hospitals.

Biography: (200 words limit)

Dr. Melissa is the one of the Department of Biomedical Engineering faculty, Vanderbilt University, Nashville, TN, United States of America, Department of Biomedical Engineering, University of Wisconsin, Madison, WI, United States of America, Morgridge Institute for Research, Madison, WI, United States of America. The Vanderbilt is comprised of 10 schools and colleges covering disciplines from the humanities to music to engineering. ... Vanderbilt is also well known for its undergraduate Blair School of Music, and the Vanderbilt University Medical Center is ranked one of the best in the nation. Former chairman and CEO of Time Inc. Department of Biomedical Engineering, Vanderbilt University, Nashville, TN, United States of America, And Conceptualization: ATS MCS. Formal analysis: ATS TMH. Funding acquisition: MCS. Investigation: ATS. Methodology: ATS TMH. Resources: MCS. Software: ATS TMH. Supervision: MCS. Validation: ATS. Visualization: ATS TMH. Writing – original draft: ATS. Writing – review & editing: ATS TMH MCSDepartment of Biomedical Engineering, University of Wisconsin, Madison, WI, United States of America, Morgridge Institute for Research, Madison, WI, United States of America.

About University (200 words limit)

The Vanderbilt University (informally Vandy or VU) is a private research university in Nashville, Tennessee. Founded in 1873, it was named in honor of shipping and rail magnate Cornelius Vanderbilt, who provided the school its initial $1-million endowment; Vanderbilt hoped that his gift and the greater work of the university would help to heal the sectional wounds inflicted by the Civil War.

Vanderbilt enrolls approximately 13,800 students from the US and over 100 foreign countries. It is classified among "R1: Doctoral Universities – Very high research activity".[9] Several research centers and institutes are affiliated with the university, including the Robert Penn Warren Center for the Humanities, the Freedom Forum First Amendment Center, and Dyer Observatory. Vanderbilt University Medical Center, formerly part of the university, became a separate institution in 2016. With the exception of the off-campus observatory, all of the university's facilities are situated on its 330-acre (1.3 km2) campus in the heart of Nashville, 1.5 miles (2.4 km) from downtown. The Fugitives and Southern Agrarians were based at the university in the first half of the 20th century and helped revive Southern literature among others.Vanderbilt is a founding member of the Southeastern Conference and has been the conference's only private school since 1966.

Vanderbilt alumni, faculty, and staff have included 54 current and former members of the United States Congress, 18 U.S. Ambassadors, 13 governors, eleven billionaires, seven Nobel Prize laureates, two Vice Presidents of the United States, and two U.S. Supreme Court Justices. Other notable alumni include three Pulitzer Prize winners, 27 Rhodes Scholars,two Academy Award winners, one Grammy Award winner, six MacArthur Fellows, four foreign heads of state, and five Olympic medallists. Vanderbilt has more than 145,000 alumni, with 40 alumni clubs established world widebrings

Importance of Research (200 words limit)

The present study was undertaken in the Radiotherapy and Otolaryngology departments of the Postgraduate Institute of Medical Education and Research (PGIMER), a tertiary care institute located in Chandigarh, India. With regards to cancer treatment, there is a provision of surgical care, chemotherapy and radiotherapy. Specifically, the radiotherapy department has 10 oncologists, 23 resident doctors, 6 medical physicists and 27 technical staff members (senior and junior technicians) and 5250 patients received radiotherapy either alone or with chemotherapy during 2014–15. Six radiotherapy machines, 2 using Cobalt-60, 4 using linear accelerators (2 Low energy 6 MV x-ray machines (DBX), 1 Dual high energy (6 MV and 15 MV) x-ray machine (DHX) and 1 image guided radiotherapy machine (IGRT) of high energy x-ray (6 MV and 15 MV)), 2 CT simulators and one conventional simulator were used for providingCapital expenditure was annualized to arrive at the equivalent annual cost taking into consideration the discount rate (time preference for money and inflation) and the lifespan of the capital equipment. A five percent discount rate was used. For some of the staff members (oncologist, nurses), who were jointly involved in a number of activities (outpatient or inpatient care, planning or delivery), cost allocation to the particular activity were apportioned based on the proportional time contribution towards each of these activities, and then multiplying it with the gross salary of the staff member. Likewise, certain resources (capital or recurrent) which were jointly shared in two or more services, were apportioned using appropriate statistics as shown in Table 1. All the results in the present study are calculated in Indian National Rupees for the year 2014–15 and were also converted into USD (United States Dollars) based on the conversion rate of 1USD = 61.02 INR, as reported by the World Bank.

References

1. providingCapitaSack DA, Sack RB, Nair GB, Siddique Ak. Cholera lancet 2004; 363(9404):233-233
2. Bauernfeind A, Croisier A, Fesselet JF et al. Cholera guidelines, 2nd ed. Paris: Medecins sans Frontieres; 2004
3. National, Malaria Control, Programme. (2013). Ghana Malaria Programme Review National Malaria, German, R. R., Lee, L. M., Horan, J. M., Milstein, R. L., Pertowski, C. A., & Waller, M. N. (2001). Updated guidelines for evaluating public health surveillance systems: recommendations from the Guidelines Working Group. MMWR. Recommendations and Reports : Morbidity and Mortality Weekly Report. Recommendations and Reports / Centers for Disease Control, 50(RR-13), 1-35-7.
4. Ali M, Nelson AR, Lopez AL, Sack D. Updated global burden of cholera in endemic countries. PLoS Negl Trop Dis. 2015;9(6):1–13. https://doi.org/10.1371/journal.pntd.0003832. CAS Article Google Scholar
5. Ali M, Lopez AL, Ae You Y, Eun Kim Y, Sah B, Maskery B, Clemens J. The global burden of cholera. Bull World Health Organ. 2012;90(3):209–18. https://doi.org/10.2471/BLT.11.093427. Article PubMed PubMed Central Google Scholar
6. World Health Organization Global Task Force on Cholera Control. Overview of ending cholera: a global road map to 2030; 2017. Available from: http://www.who.int/cholera/publications/global-roadmap-summary.pdf?ua=1. [Accessed 12 Mar 2018].
7. Moore S, Miwanda B, Sadji AY, Thefenne H, Jeddi F, Rebaudet S, De Boeck H, Bidjada B, Depina JJ, Bompangue D, Abedi AA. Relationship between distinct African cholera epidemics revealed via MLVA haplotyping of 337 Vibrio cholerae isolates. PLoS neglected tropical diseases. 2015;9(6):e0003817. https://doi.org/10.1371/journal.pntd.0003817. CAS Article PubMed PubMed Central Google Scholar
8. Bwire G, Ali M, Sack DA, Nakinsige A, Naigaga M, Debes AK, Ngwa MC, Brooks WA, Orach CG. Identifying cholera "hotspots" in Uganda: an analysis of cholera surveillance data from 2011 to 2016. PLoS Negl Trop Dis. 2017;11(12):e0006118. https://doi.org/10.1371/journal.pntd.0006118. Article PubMed PubMed Central Google Scholar