

#### **Study Title**

Evaluating the Impact of the Audio-Visual Assisted Therapeutic Ambience in Radiotherapy (AVATAR) System Versus Anesthesia for Motion Management in Pediatric Patients with Wilms' Tumor Undergoing Radiation Therapy

#### **Protocol Number:**

IUSCCC-0961

#### **Coordinating Center:**

Indiana University Simon Comprehensive Cancer Center

#### **Principal Investigator:**

Jordan Holmes, MD, MPH

jorholme@iu.edu

IU Health Department of Radiation Oncology
535 Barnhill Drive RT 041
Indianapolis, IN 46202
(317) 944-2524

#### **Co-Investigators:**

Sarah Akinterinwa Megan Sloan Emerson Taylor Emilee Wilson Megan Knight

#### **Protocol Version Date:**

5 September 2025

**Purpose:** To evaluate intrafraction motion in pediatric patients with Wilms' tumors (nephroblastoma) treated with either the Audio-Visual Assisted Therapeutic Ambience in Radiotherapy (AVATAR) distraction or general anesthesia (GA), assessing whether AVATAR can provide equivalent immobilization while reducing anesthesia-related risks.

Methods: A retrospective analysis was conducted from imaging data from 32 patients (20 AVATAR, 12 GA) at Indiana University Health Simon Cancer Center between February 11, 2019, and July 31, 2025. Motion parameters were measured using paired kilovoltage (kV) and megavoltage (MV) images from an offline review platform. The horizontal and vertical shifts of the treatment isocenter relative to vertebral landmarks were quantified to assess intrafraction motion. Measurements were independently verified by four reviewers, and differences were then averaged. A statistical comparison between AVATAR and GA groups was done using an independent t-test.

**Results:** Mean horizontal and vertical displacements for AVATAR patients were  $0.265 \pm 0.255$  cm and  $0.201 \pm 0.159$  cm, compared with  $0.280 \pm 0.284$  cm and  $0.290 \pm 0.328$  cm for GA patients. Observer variability was minimal at an average of 0.159 cm. Imaging times were comparable between AVATAR (mean 7 minutes 42 seconds) and GA (mean 7 minutes 27 seconds) patients. The independent two-sample t-test produced a p-value of 0.833 for the horizontal shifts and 0.232 for the vertical shifts.

**Discussion:** Given the results of the t-tests, the analysis indicated no statistically or clinically meaningful differences between the two techniques for both the horizontal and vertical shifts. Because of this, the AVATAR system provided effective intrafraction immobilization compared to the GA technique. Age differences between the two groups were likely contributing to compliance; however, the overlapping age ranges indicate that motion control was not exclusively age dependent. The AVATAR system did not significantly impact workflow, suggesting if incorporated into institutions the technique could be used within daily treatment without delays. These findings do align with previous research studies showing AVATAR's ability to reduce anesthesia while maintaining treatment accuracy. Limitations include a small sample size, assessment of motion only through static imaging, and inability to measure full setup times.

**Conclusion:** AVATAR is an effective, non-invasive alternative to anesthesia for pediatric patients with Wilms' tumors, providing comparable immobilization while also reducing

anesthesia-related risks. The integration of this distraction system into pediatric radiation therapy can improve safety, efficiency, and overall patient experience.

## Introduction

Radiation therapy for pediatric patients presents unique challenges due to the difficulty of immobilizing young patients during imaging and treatment delivery. Immobilization is critical, as even small movements can compromise treatment effectiveness, increase radiation exposure, and prolong treatment time. The standard method to minimize motion in younger children is general anesthesia (GA) as it is a reliable source to reproduce immobility. However, this approach carries medical risks, increased resource utilization and treatment duration, and additional financial burdens on families.

As found in multiple studies, there are many clinical concerns when it comes to prescribing general anesthesia for pediatric patients in the imaging world. Beyond the fact that anesthesia is a cost burden to families and causes psychological distress for pediatric patients, there is research that proves GA could be associated with numerous risks and side effects. The reason this occurs is because, compared to adults, infants have several anatomical and physiological differences – making pediatric anesthesia complicated. Early data which remains prevalent shows that the most frequent complications of GA are drug-induced cardiorespiratory depression, which includes "upper-airway obstruction, hypoventilation, hypoxia, and hypotension". In addition to these immediate concerns, other post-anesthetic symptoms such as "post-sedation nausea, vomiting, disorientation, sleep disturbance, and nightmares" are relatively common. Furthermore, evidence indicates that the "use of three or more sedative drugs significantly increases the rate of adverse outcomes." (Arlachov & Ganatra, 2012) Because of these drawbacks, institutions started looking for alternative methods to minimize motion that can either reduce or fully eliminate the need for anesthesia during radiation therapy, while improving the overall quality of care given.

One promising advancement is the Audio-Visual Assisted Therapeutic Ambience in Radiotherapy (AVATAR) system. The AVATAR distraction is a radiation—compatible audiovisual distraction device that places a radiolucent screen displaying customized video content that is liked by the patient. The patients can watch videos directly above them during the simulation and within each treatment fraction to create a more calming environment. For the

treatment of pediatric patients with Wilms tumors, the standard setup approach is to place them in a supine position (laying on their back) in a custom full body vaclock with their arms above their head, along with an immobilization belt for safety precautions. The AVATAR distraction aims to grab the attention of the patient and keep them calm so that immobilization can be tolerable rather than turning to daily anesthesia.

There are several published studies that have reported encouraging results when looking into the implementation of the AVATAR distraction. There are four articles that were reviewed, which will be discussed in the literature review; establishing AVATAR is a feasible and promising tool for immobilizing pediatric patients and reducing the need for anesthesia. Together, the articles demonstrate that many pediatric patients have been successful in completing their treatment courses when AVATAR was implemented and highlight improvements in patient comfort. Despite these results, most published articles focus primarily on cost savings or other benefits rather than motion control itself. Although AVATAR is a widely known technique, there is not much data about the effectiveness of immobilization using the AVATAR distraction. Along with the literature review, Indiana Health University Hospital has used the AVATAR distraction system for several years, showing that pediatric patients can complete their treatment without anesthesia. Despite information available from both sources, there remains limited comparative evidence of whether the AVATAR distraction can achieve the level of intrafraction immobilization that equates anesthesia in pediatric populations.

To build on existing research, this study will analyze previously acquired data from pediatric patients with Wilms' tumors (nephroblastoma) that were treated with either AVATAR or anesthesia. This study focuses on addressing the gap in knowledge of the intrafraction motion by comparing the use of anesthesia with the non-pharmacologic AVATAR system among pediatric patients receiving radiation therapy for Wilms' tumors. These findings have the potential to support the adoption of the AVATAR system as a motion management distraction system that overall enhances patients' safety, reduces setup time, and minimizes not only anesthesia but also radiation exposure.

#### **Review of Literature**

The study by Hiniker et al, titled *Initial Clinical Outcomes of Audiovisual-Assisted*Therapeutic Ambience in Radiation Therapy (AVATAR), evaluated an audiovisual system that

allowed pediatric patients to watch video content during radiation therapy. The results showed that most patients could complete their radiation treatments without sedation and without compromising treatment accuracy. The findings indicated that audiovisual distraction is safe, reduces anxiety, and increases cooperation. Other studies have supported the use of distractions for motion reduction and patient comfort, but few directly compare AVATAR with general anesthesia. The in-room screen of the AVATAR system plays age-related videos or animations that would assist in creating an ambiance that may make the patient indifferent to the procedure. Therefore, this research study compares AVATAR with anesthesia in terms of the extent to which it provides motion control, with side effects involving less invasiveness, safety, and discomfort for young patients. The results might imply a better approach toward radiation therapy in future pediatric cases and decrease the need for anesthesia in clinical practice.

In the study by Ritchie, Pediatric radiation therapy without anesthesia – Are the children moving, the researcher discussed pediatric radiation therapy without the use of general anesthesia. The study assessed the feasibility of treating children "awake" during radiation therapy, examining workflow, patient compliance, motion, and other practical considerations when anesthesia was not used. It was demonstrated in the outcomes that suitably based radiation therapy, in children, can beneficially be performed safely and successfully, without administration of anesthesia. Emphasis was placed by the authors, in connection with this procedure, on the essential provision of appropriate support in the way of immobilization, diversion, and a child-centered workflow. This article is relevant to the study because it focuses on motion management and non-anesthesia alternatives in pediatric radiotherapy. While Ritchie explored the broader concept of awake treatment, the study did not directly compare a distraction-based system such as the Audio-Visual Therapeutic Ambience in Radiotherapy (AVATAR) system to anesthesia, nor did it focus on a single patient population like those with Wilms tumors. The study builds this work by directly comparing intrafraction motion outcomes between children treated with the AVATAR system and those treated under general anesthesia at a single institution. By focusing on a uniform diagnosis and incorporating detailed motion measurements using paired kV and MV images, the research extends Ritchie's findings to a more specific clinical scenario, providing quantitative data on the effectiveness of distraction systems versus anesthesia in motion control.

In the study by Prasad et al, titled *Radiation Therapy Without Anesthesia for a 2-Year-Old Using Audio-Visual Assisted Therapeutic Ambience in Radiation Therapy (AVATAR)*, the authors described young male patients diagnosed with stage IV Wilms' tumor that was treated for a bilateral whole-lung and left flank radiation therapy plan. To prevent general anesthesia, a video distraction - AVATAR - was used during treatment sessions. The anxiety of the child, defined by the modified Yale preoperative Anxiety Scale or mYPAS, was very high in simulation (14/18) and the treatment time was shortened by approximately 66% from 90 to 30 minutes with AVATAR. This article aims to establish the extension of AVATAR in younger patients that previously tested studies at the time that had not incorporated one under 3 years old. This had several advantages including reduced cost, reduced risk of anesthesia and toxic effects, and better experience for patients and their families.

The researchers in this study, Balazy et al., wrote a paper titled Impact of Audiovisual-Assisted Therapeutic Ambience in Radiation Therapy (AVATAR) on Anesthesia Use, Payer Charges, and Treatment Time in Pediatric Patients, that focused on investigating the usefulness of combining audiovisual-assisted therapeutic ambience (AVATAR) with radiation therapy sessions in patients. The study aimed at establishing whether audiovisual distraction tools (music, videos, and room projections) could decrease the treatment time, lower payment expenses without influencing the precision of the treatment and patient results and lessen the necessity of anesthesia. The researchers compared results of the treatments administered to pediatric patients who went through the standard radiation therapy procedures with those who administered therapy complemented with AVATAR. The outcomes revealed that there was a significant reduction in the use of the anesthesia among the patients who had been exposed to the AVATAR system, which resulted in a reduction in the length of treatment and a significant decrease in the healthcare expenses. Besides, the study discovered that AVATAR enhanced patient compliance and comfort, which generated a less stressful therapeutic setting that reduced the emotional distress most pediatric patients were usually subjected to throughout radiation therapy. This study is important since it emphasizes the ability of non-pharmacological interventions to improve the quality of treatments, their efficiency, and safety. The decrease in the medical risk caused by multiple sedation attempts combined with anesthesia helps reduce the error risk in clinical practice and simplifies clinical work and reduces costs at the institution.

Moreover, AVATAR can ensure better adherence and comfort of patients, which makes treatment delivery more uniform and refined.

In addition, these findings may offer larger suggestions for clinical practice by aiding in identifying the conditions under which AVATAR can be viewed as a reliable substitute for anesthesia without affecting or compromising motion control or its precision. By reducing the reliance on anesthesia not only is it able to reduce the pharmacologic risks, but it also may reduce treatment, and the improvement of the overall workflow efficiency in treating pediatric Wilm's tumors. Finally, research may serve as a foundation for prospective studies in the future that are aimed at standardizing AVATAR-based protocols that extend across a wider range of pediatric treatment sites, focusing and furthering a more advanced, patient-centered approach in pediatric radiation therapy.

#### **Methods**

The study was a retrospective evaluation of pediatric patients with Wilms tumors who received external beam radiation therapy (EBRT) at Indiana University Health Simon Cancer Center between February 11, 2019 and July 31, 2025. This study was aimed at comparing the application of the AVATAR system with general anesthesia in intrafraction motion management during treatment.

The patients were separated into two groups: 20 patients received treatment using the AVATAR distraction, and 12 patients received treatment under general anesthesia. To ensure that this study was clinically relevant, the study needed to include pediatric patients who would be comparable in terms of cooperation level, need for anesthesia, and anatomical considerations. Because of this, pediatric patients that were under the age of 3 and above the age of 10 were excluded from the study. Patients under 3 years old generally cannot tolerate the AVATAR distraction technique as very young children almost always require GA – including them would bias the comparison since most would not be eligible for AVATAR. On the other hand, patients over 10 years old naturally have better cooperation, making GA more rarely used. Along with that, older patients also have different anatomy which may require additional immobilization or imaging protocols. Patients were also excluded if they had poor imaging quality; therefore, it was insufficient to obtain an accurate measurement. The group of patients chosen for this study were

based on the inclusion criteria of an AP and/or PA treatment and imaging set and diagnosis of Wilms' tumors as well as the presence of matched kV and MV images on the first day of treatment. Patients with nephroblastoma's are typically treated with opposed anterior/posterior (AP) or posterior/anterior (PA) fields along with daily alignment verification using orthogonal kV images that are being matched to bony landmarks. Traditionally, on the first day of treatment, MV imaging is acquired for additional verification, which allows the unique opportunity to measure patient shifts between the kV and MV image sets.

Based on the literature reviewed, most studies defined the start time as the time documented in record at which the final couch shift corrections were applied after kV setup imaging. The definition of the end time was noted as the timestamp of the last MV portal image acquisition of the AP/PA fields for that fraction. Because of this, that approach was adopted in this study for the consistency of results. Overall, the time elapsed between the kV image (to verify initial setup) and the MV image (to verify final positioning) was retrieved through metadata of the image.

Motion parameters were obtained independently by four reviewers, and differences between observers were then assessed and averaged. Measurements were taken by determining the treatment isocenter from the online matched graticule and the nearest visible vertebrae on each image. The horizontal and vertical measurements of the isocenter against the vertebral edge on the kV and MV images were taken. The difference between the two sets of measurements on the two axes was intrafraction motion in centimeters (cm). The calibrated ruler tool was used to measure in the image review software (e.g., ARIA Offline Review) as well as precise acquisition times were obtained using the DICOM metadata of every image.

To analyze the differences in motion between the two immobilization techniques – AVATAR and GA – an independent t-test was performed for both horizontal and vertical measurements. A t-test is a statistical test that compares the average motion of two groups to evaluate whether the shifts were statistically significant. The t-test calculates a p-value indicating "the probability of obtaining data equal to or more extreme than the data (results) observed, given that the null hypothesis is true" (Boscardin, 2024). If the p-value is below the threshold of 0.05, the difference is considered statistically significant – meaning that it is unlikely due to chance. On the other hand, if the p-value is above 0.05, the groups are considered statistically

similar. Using the t-test helps to determine if the motion differences were meaningful from a statistical standpoint.

## **Results**

A total of 32 pediatric patients, aged 3-10 years, underwent radiation therapy (EBRT) for Wilms' tumors at Indiana University Health Hospital between February 2019 and July 2025. Of these, 20 patients (62.5%) were treated using the AVATAR technique, while 12 patients (37.5%) were treated under general anesthesia (GA) (Figure 1). The median age for the patients in the AVATAR group was 5 years old (range: 3-9 years), compared with a median age of 4 years (range 3-6 years) in the GA group (Figure 1). Overall, within the study, patients that received the AVATAR distraction technique tended to be slightly older than those who required GA; therefore, being consistent with the clinical observation that younger children are less likely to tolerate radiation without GA. Although the age ranges between the two groups overlap, the AVATAR group included more patients that were 6 years or older suggesting there is a relationship between age and the ability to cooperate with the audio-visual distraction technique.

To support the study's primary objective, Figure 2 presents the mean horizontal and vertical intrafractional shifts for both AVATAR and GA groups. The average motion that was observed with the AVATAR technique was 0.265 +/- SD 0.255 cm in the horizontal direction and 0.201 +/- SD .159 cm in the vertical direction. On the other hand, for patients under GA the mean horizontal and vertical shifts were 0.280 +/- SD 0.284 cm and 0.290 +/- SD 0.328 cm. As explained in the methods section, 4 observers cross measured all the data to ensure uniformity and reliability. Across all measurements, the average observer difference was minimal, 0.159 cm difference (all under 0.270 cm) which supports the consistency in the data collection process (Figure 3). A two-sample t-test was performed in Excel that demonstrates no statistically significant difference between the two groups for horizontal (p = 0.833) or vertical motion (p = 0.232). Even though there were minor variations in average motion observed throughout all the patients, the findings indicate both AVATAR and GA to provide effective immobilization for CT simulation and treatment accuracy.

Along with the primary objective of evaluating the intrafraction motion of the AVATAR system comparable to the use of anesthesia, the imaging and treatment times were assessed between the two groups. The average time between imaging for AVATAR patients was 7

minutes 42 seconds (range: 1 minute 41 seconds- 21 minutes 26 seconds), compared to GA patients with 7 minutes 27 seconds (range: 1 minute 55 seconds – 15 minutes 16 seconds). Individual times did vary slightly due to factors such as patient cooperation and setup differences.

# **Discussion**

The results of this retrospective research study suggest that the AVATAR distraction provides minimal intrafraction motion and overall effective motion management that is comparable to general anesthesia in pediatric patients with Wilms' tumors. To start, the age differences between the two groups provide context when interpreting these findings. The children who were treated with the AVATAR distraction were generally older (median age 5 years old) than those who were treated under general anesthesia (median age 4 years old), which relates with known patterns within a clinical setting. Older children typically have longer attention spans and lower levels of anxiety when it comes to treatment. This allows older patients to remain still without the use of anesthesia and vice versa for younger children. Although age is a likely contributor to immobilization during treatment, the overlapping age ranges between groups explain both techniques were applied to comparable populations and that the comparison in motion management cannot be associated with age alone.

While evaluating motion data, it is shown that horizontal and vertical intrafraction shifts were small and insignificant between groups. While there is no clearly defined standard for what intrafraction motion is acceptable in this clinical scenario, the shifts in both groups were unlikely to result in an anatomic miss of the target. AVATAR patients demonstrated average motion of 0.265 cm horizontally and 0.201 cm vertically, while general anesthesia patients had average shifts of 0.280 cm and 0.290 cm. These findings prove that the AVATAR distraction can efficiently reduce patient movement during simulation and treatment without the need for general anesthesia. The measurements were independently performed by four researchers who had interpreted their own measurements. Upon further analysis, the average observer difference was 0.159 cm, which is minimal, confirming the reproducibility of the measurements to provide a sense of confidence in the equivalence between groups.

Analyzing the time of treatment can show how well the workflow can be. Upon analyzing the times, it was discovered that there was a similarity in the time interval of imaging,

with AVATAR patients of 7 minutes 42 seconds and general anesthesia patients of 7 minutes 27 seconds, between the kV setup and verification of MV. Although AVATAR displayed a wider variability, it shows differences in how cooperative the patients were. There was overall similarity in median time proving that the audiovisual system has no effect on slowing down the process of treatment delivery. It displays that AVATAR can be added into the regular workflow with no delays, and it does not require extra time for providing anesthesia, monitoring the patient, and the recovery of the patient. Although these parameters were not directly measured, the use of AVATAR may reduce overall treatment time by eliminating the need for anesthesia, additional monitoring, and recovery. Further research studies could further examine this effect.

To determine the level of significance, the two immobilization techniques were compared using a t-test, and it was found that the p-value was 0.168, which is larger than the traditional significance value of 0.05. This result indicates that the difference in the motion between patients receiving AVATAR and general anesthesia is not significant. This has implications that the AVATAR system has very similar control of motion to that of using anesthesia. This supports the hypothesis of the study and confirms the idea that non-invasive techniques can be as accurate as immobilization with some pediatric patients.

The findings are highly correlated with journals like those by Hiniker et al., Balazy et al., and others, who found that AVATAR results in a reduction in the use of anesthesia and a reduction in the time of treatment with no effect on the actual performance of treatment. These results agree with earlier published literature, including the research by Hiniker et al, and Balazy et al., which indicated that distributed audiovisual distraction systems are capable of greatly lowering the necessity of anesthesia with no compromise of treatment accuracy. The findings build upon these findings by offering quantitative data that AVATAR does not only decrease dependence on anesthesia but also offers similar immobilization results. This is an indication that the calming and attention effects of the system can be successful in reducing motion, even in younger pediatric patients who have traditionally necessitated general anesthesia.

Altogether, this research contributes to the expanding body of literature that the AVATAR system is an efficient, non-invasive model of anesthesia compared to motion management in pediatric radiation therapy. AVATAR can improve patient experience, safety, and efficiency in the provision of pediatric radiotherapy by creating more accurate immobilization, minimizing setup time, and enhancing patient experience.

Although this research has produced some encouraging findings, there are multiple limitations that need to be acknowledged. First, the sample size was small (n = 32) which reflects the narrow inclusion criteria of age, diagnosis, and paired kV/MV images. While this approach allows uniform comparison between the two groups, it limits the generalizability of the findings. Second, intrafraction motion was assessed only using static images (kV and MV), while this gives a good idea of shifts it does not show continuous motion monitoring and cannot account for patient movement outside the lateral and vertical plane. Lastly, because only image timestamps were available, the true setup time could not be measured preventing differentiation between delays related to patient immobilization, anesthesia setup, and overall workflow between the two techniques. These factors highlight the need for additional studies with larger cohorts and real-time motion tracking systems. Despite these limitations, there were consistent patterns seen in both groups that suggest the study's results are reliable and not due to random variation.

## **Conclusion**

This study demonstrated that the AVATAR system is a useful, effective, and non-invasive tool for motion guidance during pediatric radiation therapy. The AVATAR technique provides comparable immobilization to pharmaceutical sedation while improving treatment experience and efficiency. The results have indicated that the intrafraction movement of the patient under the use of AVATAR was identical and even lower than movement of the patients under anesthesia, and all were within the clinically acceptable limits.

In addition, the use of AVATAR is extremely influential in removing the potential risk factors that come along with the use of anesthesia, lowering the physical and emotional stress of the patients, and increasing the safety of the patient. Less reliance on anesthesia will result in a shorter time of treatment, less repeat imaging, and an efficient workflow that would be necessary in a busy cancer center. The shortening of the image acquisition time of the AVATAR group shows clinically that the use of audiovisual devices can improve patient compliance and reduce the number of delays. Not only do they aid a patient to feel more relaxed, but they also influence the work of the multidisciplinary team, reducing the use of resources and lowering the overall cost of treatment.

To conclude the findings of this retrospective study, AVATAR should be considered for standard implementation in pediatric radiation therapy for Wilms' tumors. This style provides an efficient yet patient-centered solution that gives a sense of accuracy on the treatment machine as well as increases the level of safety. As technology keeps increasing, more studies using large and prospective datasets can help confirm the clinical uses of AVATAR, which will be a groundbreaking tool in the delivery of humane, accurate, and precise radiation oncology services to children.

# Figures/Tables

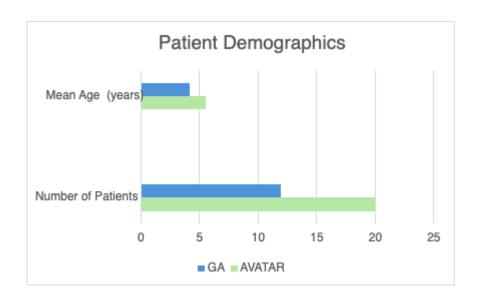
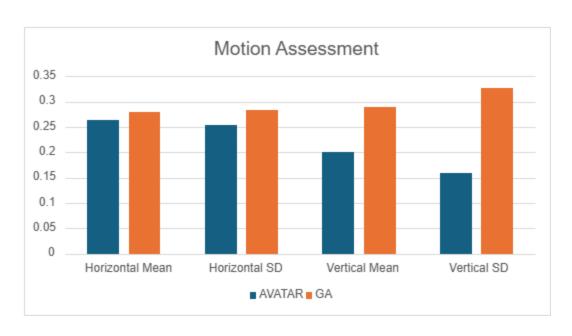
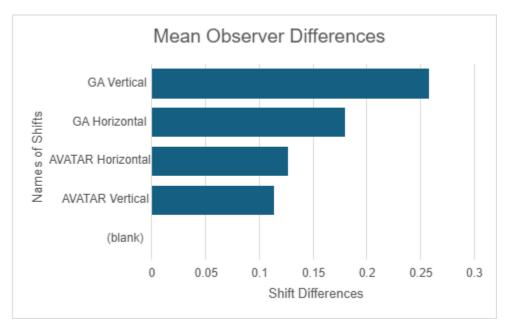


Figure #1: Demographics showing the number of patients included as well as the median age, in years, of each group – AVATAR and GA.



<u>Figure #2:</u> Motion assessment showing mean and standard deviation of horizontal and vertical shifts (cm) for AVATAR and GA.



<u>Figure #3</u>: Mean observer differences for horizontal and vertical motion (cm) across both groups.

# References

- Arlachov Y, Ganatra RH. Sedation/anaesthesia in paediatric radiology. Br J Radiol. 2012;85(1020):e1018-e1031. Accessed from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3500799/
- 2. Hiniker SM, Roeske JC, Kang HC, Kozak KR, Goldman EE. Initial clinical outcomes of audiovisual-assisted therapeutic distraction during pediatric radiation therapy. Pract Radiat Oncol. 2017;7(4):e265-e272. doi:10.1016/j.prro.2017.01.006
- 3. Ritchie J. Paediatric radiation therapy without anaesthesia. Radiother Oncol. 2024;196:109084. doi:10.1016/j.radonc.2024.109084
- 4. Prasad RN, Baliga S, Banner J, et al. Radiation therapy without anesthesia for a 2-year-old child using audio-visual assisted therapeutic ambience in radiation therapy (AVATAR). Pract Radiat Oncol. 2022;12(3):e216-e220. doi:10.1016/j.prro.2021.12.009
- 5. Balazy KE, Gutkin PM, Skinner L, et al. Impact of audiovisual-assisted therapeutic ambience in radiation therapy (AVATAR) on anesthesia use, payer charges, and treatment time in pediatric patients. Pract Radiat Oncol. 2020;10(4):e272-e279. doi:10.1016/j.prro.2019.12.009
- 6. Boscardin CK, Sewell JL, Tolsgaard MG, Pusic MV. How to use and report on p-values. Perspect Med Educ. 2024;13(1):250-254. doi:10.5334/pme.1324