Title
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Journal
International journal of radiation oncology, biology, physics, 117(1)

ISSN
0360-3016

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Publication Date
2023-03-01

DOI
10.1016/j.ijrobp.2023.03.063

Peer reviewed

Journal Pre-proof

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PII: S0360-3016(23)00307-3
DOI: https://doi.org/10.1016/j.ijrobp.2023.03.063
Reference: ROB 28163

To appear in: *International Journal of Radiation Oncology, Biology, Physics*

Received date: 23 January 2023
Revised date: 12 March 2023
Accepted date: 22 March 2023

Please cite this article as: Paulina M. Gutkin BS , Lawrie Skinner PhD , Alice Jiang BA , Sarah S. Donaldson MD , Billy W. Loo Jr., MD, PhD , Justin Oh MD , Yi Peng Wang BA , Rie von Eyben MS , John Snyder MS , Jeremy S. Bredfeldt PhD , John C. Breneman MD , Louis S. Constine MD , Austin M. Faught PhD , Daphne Haas-Kogan MD , Jordan A. Holmes MD , Matthew Krasin MD , Charlene Larkin CCLS , Karen J. Marcus MD , Peter G. Maxim PhD , Shearwood McClelland III MD , Blair Murphy MD , Joshua D. Palmer MD , Stephanie M. Perkins MD , Colette J. Shen MD , Stephanie Terezakis MD , Karl Bush PhD , Susan M. Hiniker MD , Feasibility of the Audio-Visual Assisted Therapeutic Ambience in Radiotherapy (AVATAR) system for anesthesia avoidance in pediatric patients: A multicenter trial, *International Journal of Radiation Oncology, Biology, Physics* (2023), doi: https://doi.org/10.1016/j.ijrobp.2023.03.063

Feasibility of the Audio-Visual Assisted Therapeutic Ambience in Radiotherapy (AVATAR) system for anesthesia avoidance in pediatric patients: A multicenter trial

Running title: AVATAR for anesthesia avoidance in pediatric radiotherapy

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Presented at the ASTRO Annual Meeting, San Antonio TX, October 25, 2022 as an Oral Presentation

ClinicalTrials.gov: NCT03991156

Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

Disclosures: No disclosures relevant to this work

Funding: Funded in part by a Stanford Cancer Center Clinical Innovation Award (Hiniker)

Acknowledgements: The authors would like to thank the participating patients, families, and study teams, and institutional study support including from the Albert Wilson Fellowship (Stanford University), the A.J. Hawk Fund (Ohio State University), and the Barnes-Jewish Hospital Foundation (Washington University).

Abstract

Purpose:

The AVATAR system was the first published radiotherapy (RT) compatible system to reduce the need for pediatric anesthesia through video-based distraction. We evaluate the feasibility of AVATAR implementation and effects on anesthesia use, quality of life (QoL), and anxiety in a multicenter pediatric trial.

Methods:

Pediatric patients 3-10 years of age preparing to undergo RT at 10 institutions were prospectively enrolled. Children able to undergo at least one fraction of RT using AVATAR without anesthesia were considered successful (S). Patients requiring anesthesia for their entire treatment course were non-successful (NS). PedsQL3.0 Cancer Module survey (PedsQL)

assessed QoL and was administered to the patient and guardian at RT simulation, midway through RT, and final treatment. The modified Yale Preoperative Assessment Survey Short Form (mYPAS) assessed anxiety and was performed at the same three timepoints. Success was evaluated using Chi-square test. PedsQL and mYPAS scores were assessed using mixed effects models with time points evaluated as fixed effects and a random intercept on the subject.

Results:

Eighty-one children were included; median age was 7 years. AVATAR was successful at all 10 institutions and with photon and proton RT. There were 63 (78%) S patients; anesthesia was avoided for a median of 20 fractions per patient. Success differed by age ($p=0.04$) and private versus public insurance ($p<0.001$). Both patient ($p=0.008$) and parent ($p=0.006$) PedsQL scores significantly improved over the course of RT for patients ages 5-7. Anxiety in the treatment room decreased for both S and NS patients over RT course ($p<0.001$), by age ($p<0.001$) and by S versus NS patients ($p<0.001$).

Conclusion:

In this 10-center prospective trial, anesthesia avoidance with AVATAR was 78% in children age 3-10 years, higher than among age-matched historical controls (49%, $p<0.001$). AVATAR implementation is feasible across multiple institutions and should be further studied and made available to patients who may benefit from video-based distraction.

Introduction

Modern radiotherapy (RT) techniques involve highly conformal beams requiring precise tumor targeting. Throughout a course of RT, which may extend over 4-6 weeks, patient immobilization and positioning are crucial to achieve accurate and reproducible radiation delivery and to avoid radiation damage to normal tissue. For patients who need RT to specific sites such as the head or neck, a custom-made immobilization mask is used to anchor the patient to the treatment couch. Although painless, RT may be difficult for pediatric patients to tolerate due to factors including anxiety, fear, claustrophobia, short attention span, and restlessness. As some treatment sessions can take up to 45-60 minutes, many children require daily general anesthesia for immobilization throughout RT.[1]

Measures to reduce the use of daily general anesthesia during RT are important, as daily anesthesia poses health risks, logistical challenges, and increases the cost of care. Although advancements in sedative combinations have yielded improved toxicity profiles, adverse effects of daily anesthesia may include risks of cardiopulmonary complications, vomiting, infection, and harmful effects on neurocognition and brain development.[2] In addition to the RT team, the presence and involvement of an anesthesia team is necessary to safely administer sedation during the RT simulation (sim) pretreatment planning session and daily treatment courses. Since the patient's vital signs must be monitored from outside the room while the radiation beam is on, anesthetic interventions may be delayed in the event of a complication. Intravenous lines must also be carefully placed to avoid interference with the radiation machine, posing further logistical obstacles.[3] Requirements to restrict liquids and solid food before anesthesia are burdensome for the patient and require early daytime treatments, which limit scheduling options. Furthermore, the outpatient setting and setup for anesthesia prolongs RT session times which may add additional burden to patients, families, and limit treatment availability for other patients. Costs of anesthesia are also significant, with estimated average payer charges approximately $50,000 for a 6-week course of pediatric administration during RT.[4]

The Audio-Visual Assisted Therapeutic Ambience in Radiotherapy (AVATAR) system is the first developed and published RT-compatible system to reduce the need for pediatric anesthesia during RT through video-based distraction (Figure 1) (Supplemental Video). Developed at XXX in 2015, institutional success has been previously reported.[5-7] Here, we investigate the feasibility of AVATAR implementation across multiple pediatric hospitals, the efficacy of AVATAR in reducing the need for anesthesia in children and the impact on patient quality of life (QoL) and anxiety during RT treatment at 10 institutions in a prospective multicenter trial.

Methods

English and Spanish speaking patients ages 3-10 years preparing to undergo radiation treatment at 10 institutions were prospectively enrolled (NCTXXXXXXXX). Patients were excluded if RT was planned for malignancies of the eye requiring minimal eye movement during RT, if a guardian could not assist in completing study questionnaires, or if the patient was assessed by the provider to require anesthesia for safety purposes. This study was approved by local ethics committees at all institutions and conducted in accordance with the Declaration of Helsinki. All patients and guardians provided written informed assent or consent. Anesthesia usage, as well as demographic, clinical, and radiation treatment information were recorded.

AVATAR systems were distributed to participating institutions and assembled as previously described.[6] Patients were introduced to the AVATAR system during sim setup and were able to select video of their choosing to watch from a selection of streaming video providers. Anesthesia teams were on standby at the discretion of the provider.

Quality of Life and Anxiety Assessments

Validated health QoL and anxiety assessments were administered at sim setup, halfway through the RT treatment course, and on the last day of RT. The PedsQL 3.0 Cancer Module[8] (PedsQL) was used to assess patient QoL. PedsQL reports parent and child responses on 8 dimensions (pain and hurt, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, perceived physical appearance and communication). Surveys are tailored for age groups 3-4 years, 5-7 years, and 8-10 years, and range from 22-27 questions on a 5-point Likert

scale, from 0 (never) to 4 (almost always). Questions are reverse scored and transformed to a 0-100 scale, with 0=100, 1=75, 2=50, 3=25, 4=0. Higher transformed scores indicate greater QoL. For each dimension, a mean of the transformed scores of the related questions is calculated. Total PedsQL scores are calculated by the mean of all items answered. If more than 50% of the questions corresponding to a particular dimension are not answered, the scaled scores are excluded from analysis. PedsQL was administered to parents and patients in the patient's respective age category. As per standard use of the PedsQL instrument, patients aged 3-4 years did not fill out the PedsQL survey; only the guardian filled out PedsQL for patients 3-4 years old.

The modified Yale Preoperative Anxiety Scale (mYPAS)[9] was used to assess patient anxiety at each timepoint while the patient was in the waiting room and in the RT treatment area, when the radiation mask was introduced to the patient if applicable. The mYPAS is completed by a trained observer and does not require survey completion by patient or guardian. It consists of 5 domains including anxiety, vocalizations, emotional expressivity, state of apparent arousal, and use of parents. Four domains are scored on a scale of 1 to 4 and vocalizations are scored on a scale of 1 to 6. Composite scores range from 22.92-100, with higher scores indicating increased anxiety behaviors. Patients who score over 30 are considered to have anxiety.[9]

Statistical Analysis

Intent to treat analyses were used. Patients able to tolerate at least one fraction (fx) of RT using AVATAR without anesthesia were considered successful (S), while those requiring anesthesia for their entire treatment course were non-successful (NS). Patients who withdrew from the study were included as NS. Fractional success included participants who did not withdraw from the study and was defined as the proportion of fractions used without anesthesia. Institutional success was defined as having 50% or more S patients. Success was evaluated using Chi-square test. PedsQL and mYPAS scores were assessed using mixed effects models with time points evaluated as fixed effects and a random intercept on the subject. For PedsQL surveys, due to low survey response rates among the 18 NS patients, only S patient survey responses were included in statistical analyses. Survey scores were analyzed by age category, survey, and

survey sub-category: ages 5-7 and 8-10 for patient PedsQL and ages 3-4, 5-7, and 8-10 for guardian PedsQL and mYPAS; and “pain and hurt”, “nausea”, “procedural anxiety”, “treatment anxiety”, “worry”, “cognitive problems”, “perceived physical appearance” and “communication.” Analyses were completed using Prism (v9; GraphPad, San Diego, CA) and R (v3.6.4, R Foundation for Statistical Computing, Vienna, Austria).

Results

From August 2019 to February 2022, 81 children from 10 institutions were enrolled in this study. After enrollment, 7 patients withdrew consent leaving 74 patients. Median age was 7 years (range 3-10). Demographic information, tumor location, and treatment intent are outlined in **Table 1**. Most patients (44.4%) were ages 5-7 years, with 40.7% ages 8-10 years and 13.6% ages 3-4 years. Over half of patients (58%) were treated to the brain and/or spine.

There were 63 (78%) S patients and 18 (22%) NS patients. Anesthesia avoidance was observed in 54.5% patients ages 3-4, 80.6% patients ages 5-7, and 84.8% patients ages 8-10. AVATAR was successful at all 10 institutions, with both photon and proton RT. Median number of treatment fractions was 28 (range 3-42). Anesthesia was avoided for a median of 20 fx per patient (range 0-38). Fourteen patients required anesthesia for the first RT fx. Of these, 6 successfully switched to AVATAR within 1-14 fx. Fractional success for all patients was 85% (1372 of 1616 fx), 74% (139 of 189 fx) for patients ages 3-4, 86% (671 of 785 fx) for patients ages 5-7, and 88% (562 out of 642) for patients ages 8-10. Of S patients, fractional success was 97% (1372 of 1410 fx). Success with AVATAR differed by age ($p=0.04$) and private versus public insurance ($p<0.001$). Success rates did not differ by institution, gender, race, treatment site or intent, or need for modifications.

Treatment modifications were required for 4 patients. These included dosimetric or AVATAR adjustments. For one patient, dosimetry created an RT plan to specifically avoid sagittal arcs due to the presence of the AVATAR system, however, this did not interfere with dosing to the

patient's tumor. This patient later withdrew from the study. The other 3 patients requiring modification were successful. At one institution, video was projected on the tunnel of a tomotherapy machine, as the arm of the AVATAR system was too large. At an institution using proton RT, the AVATAR system did not fit onto the head of the treatment couch. Attaching AVATAR elsewhere caused the video to project upside down, thus a laptop was required to manually orient the video to the patient. One patient used AVATAR for the entire initial prescribed treatment course, however, AVATAR could not be used for the boost plan due to the angle of the RT beam because the posterior superiorly oriented beam could not be angled to avoid the AVATAR projector.

A summary of PedsQL Patient Report survey responses is included in **Table 2**. Of S patients eligible to take the PedsQL surveys (those aged 5-10 years), all 29 (100%) patients ages 5-7 and 26 of 28 (93%) patients ages 8-10 completed more than 50% of surveys and were included in survey analysis. Total PedsQL scores significantly improved over the RT course for children ages 5-7 ($p=0.0078$) but remained constant for those 8-10 years ($p=0.52$). For 5–7-year-olds, treatment anxiety ($p=0.01$) and perceived physical appearance ($p=0.001$) significantly improved over the course of RT. For patients ages 8-10, treatment anxiety significantly improved over RT ($p=0.02$). Patient QoL scores for procedural anxiety were lower than other survey dimensions.

Guardian survey scores are summarized in **Table 3**. Overall, guardians reported that patient QoL significantly increased over RT for patients aged 5-7 ($p=0.006$). Guardians reported significant improvement in patient QoL for those 5-7 years in the categories of pain and hurt ($p=0.01$), procedural anxiety ($p=0.04$), and treatment anxiety ($p=0.04$). There were no significant trends over RT for patients ages 3-4 or 8-10. Scores for procedural anxiety and treatment anxiety were lower for patients of all ages, compared to other survey dimensions.

Anxiety scores measured by mYPAS for all patients are depicted in **Figure 2**. Anxiety significantly decreased over the course of RT ($p=0.0006$) for all ages, more for S patients than NS, and anxiety scores were most influenced in the treatment room (away from parents/guardians)

(**Figure 2C**). Anxiety was also significantly lower in S patients compared to NS patients (p<0.001) and was lower in older compared to younger patients (p<0.001). Anxiety scores assessed in the waiting room decreased over the RT course (p=0.02) but did not differ by success using AVATAR or age category.

The 6 patients who initially required anesthesia for the first RT fx and were able to transition to AVATAR were ages 3 (1 patient), 5 (2 patients), 6 (2 patients) and 9 years (1 patient). PedsQL Parent scores for the 3-year-old at the simulation, midpoint, and final treatment timepoints were 79.3, 88.2, and 81.8, respectively. Mean PedsQL Patient scores for the patients ages 5 and 6 at each timepoint 74.1, 80.4, and 86.9. PedsQL Patient scores for the 9-year-old at each timepoint were 70.6, 77.9, and 67.1. The total mean mYPAS scores for all 6 of these patients at each timepoint were 33.7, 26.2, and 27.3.

Discussion

Repeated anesthesia use during radiotherapy carries health and development risks, poses logistical treatment challenges, and carries high costs. AVATAR is a novel system with a radiolucent screen through which the radiation beam can pass with negligible attenuation that enables patients to divert their attention away from RT treatment, improving comfortability while maintaining immobility. This is the first report of successful use of the AVATAR system across multiple institutions using both photon and proton RT, with avoidance of anesthesia in 78% (63 of 81) children between the ages of 3-10 years.

Three existing reports in the literature have previously described rates of anesthesia use during radiation by age for patients between 3-10 years, including four total cohorts (one report describing two cohorts, before and after the introduction of a child life specialist).[1,4,6] Compared to these four patient cohorts of children age 3-10 years with overall anesthesia avoidance rate of 49%, the rates of anesthesia avoidance in the AVATAR multicenter study were significantly higher (78%, versus 36%[1], 42%[4], 60%[6], and 61%[4], p<0.001). The most pronounced differences

in anesthesia rates were seen in the younger patients (ages 3-4 years: 55% anesthesia avoidance with AVATAR, versus 0%[4], 2%[1], 3%[4], and 11%[6], p<0.001; ages 5-7 years: 81% anesthesia avoidance with AVATAR versus 27%[4], 35%[1], 59%[6], and 67%[4], p=0.02).

Retrospective single institution analyses of anesthesia use during pediatric RT before and after AVATAR introduction has been previously described. Hiniker et al.[5] initially reported that 92% (23 of 25) patients were able to successfully complete their prescribed RT course without anesthesia using AVATAR. Balazy et al.[6] compared patients 3-12 years of age treated with RT over a 3-year timeframe after the introduction of AVATAR to age-matched controls treated over the span of 3 years before AVATAR. Significantly reduced average RT treatment times were found following the implementation of AVATAR, from 36.7 minutes without AVATAR to 22.6 minutes with AVATAR. A 16% reduction in anesthesia use during RT treatment sessions was observed in patients after AVATAR was introduced compared to prior. Additionally, a significantly greater proportion of patients were able to completely avoid anesthesia during radiation after AVATAR (73.2%), compared to before (63.4%, p=0.03). Prior to AVATAR, 38.3% of treatment sessions required anesthesia, and use was significantly reduced to 22.1% after AVATAR.[6] Across all patients in the present multicenter study, we observed anesthesia use in only 12% of 1616 treatment sessions.

Older age is associated with lower anesthesia use. In our institutional work analyzing anesthesia use prior to the introduction of AVATAR, the proportion of treatment sessions requiring anesthesia was 88% in patients ages 3-4, 56% for ages 5-7, and 13% for ages 8-12.[6] These proportions significantly decreased with AVATAR to 61%, 35%, and 0%, respectively.[6] McMullen et al.[1] found that anesthesia use was required in over 90% of patients aged 3-4 years, 65% of those 5-7 years, and 38% of those 8-10 years. In this present study, we observed anesthesia use for the entirety of RT in 26%, 15%, and 12% for patients ages 3-4, 5-7, and 8-10 years, respectively. Of note, though our initial institutional experience included patients up to age 12 years, the maximum age included in this study was 10 years, because of our previous findings that 11–12-year-olds were very unlikely to require anesthesia.

Select patients who present with developmental delays or special needs may especially benefit from the AVATAR system. Gutkin et al.[7] reported successful implementation of AVATAR for a previously combative patient with trisomy 21 and diabetes insipidus treated with RT to the brain. Avoidance of anesthesia was particularly advantageous in this case as comorbidities associated with trisomy 21 elevate the risk of anesthesia complications. Most recently, a 2-year-old patient, ineligible for participation in the present study due to very young age but treated as per protocol, was described to successfully use AVATAR without anesthesia for his entire treatment course.[10] This patient's treatment time was decreased from 90 to 30 minutes and his mYPAS anxiety score significantly decreased from sim setup to last treatment day. These two reports indicate the promise for AVATAR use in select patients who likely would have historically required anesthesia.

Cost effectiveness of AVATAR has also been described. Scott et al.[4] reported an average cost of anesthesia for a 6-week (30-day) course of RT of $50,000, equating to $1,667 per treatment session. Modeling these figures, Balazy et al.[6] reported an estimated $543,333 in savings with the avoidance of anesthesia in 326 treatment sessions with AVATAR. One study analyzing cost savings during the treatment of 2 patients reported the cost of pediatric anesthesia to be $1,904 per RT fraction and $38,087 per patient for a 4-week treatment course, including sim setup.[11] Using cost estimates from Scott et al., savings in the present study are estimated to be $2,287,124 for the 1372 fractions in which anesthesia was avoided. It is worth noting that the out-of-pocket charge to the patient and the amount paid by insurance are often significantly less than payer charges noted above and are related to a myriad of factors including insurance coverage, reimbursement model, and other third-party payer coverage. Nevertheless, the use of anesthesia for RT carries significant expense that can be meaningfully reduced with implementation of the AVATAR system. In contrast to anesthesia, implementation of AVATAR is relatively low cost, with the cost of each system approximately $500. In the present study, institutions continued their standard of care practices in addition to AVATAR, which varied across institutions and for some institutions involved assistance from existing departmental

certified child life specialists (CCLS). Additional assistance with system set up was provided by each institution's physics and radiation therapist teams. Despite differences in institutional practices, all institutions were successful with AVATAR (> 50% S patients).

Other methods of attempting to reduce the need for anesthesia during radiation have been described and include use of CCLS, psychoeducation, and mounted television screens outside of the radiation beam path.[4,12-14] The AVATAR system is unique to these methods; its flexibility, ease of set up, capability of playing patient-selected videos, and ability to lie within the field of the patient's vision without interfering with radiation administration make AVATAR more accessible for expanded use.

In this study, we found decreased anxiety, as reported by study personnel, as well as improved patient and parent quality of life throughout the course of RT. To our knowledge, no previous study has reported anxiety scores using mYPAS at serial timepoints throughout the pediatric radiation course. In a study of pre-operative sedation among children ages 2-12, Kim et al.[15] report that mYPAS anxiety scores greater than 40, younger age, and long wait times predicted the need for pre-operative sedation. In line with this, it is worth noting that most patients in our study had anxiety (scores over 30) and that most S patients had scores under 40 throughout treatment, while more NS patients had scores over 40. This disparity may suggest patients who have high baseline anxiety may be less likely to successfully avoid anesthesia with AVATAR. Consistent with our findings, Lee et al. described the use of cartoon distraction in reducing child anxiety during preoperative anesthesia induction.[16] Of note, we observed 6 patients who initially required anesthesia but were eventually successfully transitioned to AVATAR. While the number of patients in this group is too small to make meaningful comparisons, our results suggest that gradual introduction of the system may be worthwhile particularly for patients with borderline baseline quality of life and/or anxiety scores. It is important to note that with repetition of RT and subsequent increased patient familiarity with the RT treatment process, it is anticipated that patient anxiety is likely to improve in some capacity throughout the treatment course independent of intervention. In the present study, attenuation of anxiety

occurred in parallel fashion across all age groups and improved in both S and NS patients. Few studies of quality of life report on multiple timepoints during pediatric radiation therapy. Kuhlthau et al.[17] report PedsQL scores at the beginning and end of proton RT in addition to longer term follow up and found marginally higher patient and parent PedsQL scores at the end of the RT course, though with slightly lower total core PedsQL scores than in our study. Though minimally studied to date, it is possible that pediatric QoL during RT may improve over the RT course as children become more accustomed to treatment, despite the fact that RT-related side effects are also increasing over this time period. The improvement of QoL and reduction of anxiety we observed during the RT course, most notably in patients ages 5-7 years, and to what extent AVATAR influences this improvement, is worthy of further investigation.

Our study was limited by delayed accrual due to the COVID-19 pandemic, which required most institutions in this study to temporarily cease clinical trial accruals. Patients were also screened by enrollment based on the provider's assessment of whether the patient could be safely treated without anesthesia; patients in whom attempts without anesthesia would pose harm to the patient were excluded, which may potentially inflate success rates. While survey completion rates were excellent, there was insufficient Peds QL survey data available from the NS patients between ages 5-10 to analyze and compare this data to that of S patients, though anxiety scores using mYPAS were available and analyzed for all patients, S and NS.

Limitations with the use of AVATAR exist, and consideration of RT beam angles and patient movement are important. Radiation treatment of brain tumors often requires the use of noncoplanar beams. While the AVATAR system is relatively small and is adjustable, it is possible that the projector for AVATAR may interfere with the posterior superior beam when mounted at the head of the treatment table; we have since developed modifications that allow mounting of the projector to other parts of the table to avoid this issue. Additionally, the AVATAR screen arm may interfere with the RT treatment arm if there is limited space between the arm and treatment bed. As with one of the patients in the study, projecting the image directly onto the tunnel of the RT machine (or the ceiling of the vault) is an appropriate alternative. In this study,

we found that no patients received modifications to their treatment plan that included use of a larger PTV margin because of use of AVATAR. However, it is important to ensure that patients can remain immobilized while using AVATAR, and practice sessions may be helpful. In instances where adequate time and support to introduce the system to an initially uncooperative patient are lacking, AVATAR may not be successful. With increased provider experience, however, patients who are borderline successful may have increased likelihood of becoming successful with AVATAR.

Contraindications for AVATAR are few but include RT to areas where treatment requires minimal eye movement. In addition, the AVATAR screen must be positioned with care in treatments utilizing surface guided radiation therapy that rely on cameras to track patient movement, as the AVATAR screen may occlude tracking depending on the location of the screen placement. This barrier may be eliminated, however, by projecting the video image directly on the treatment tunnel or ceiling.

This was a collaborative multicenter trial including patients from 10 institutions, independent of any existing pediatric radiotherapy consortium. Further studying and expanding the use of AVATAR to patients who may benefit from video distraction, including in the adult population, and in resource-limited areas where access to anesthesia is less, are needed.

Conclusion

Across 10 centers, anesthesia avoidance with AVATAR was 78% among children age 3-10 years, significantly higher than anesthesia avoidance in age-matched historical controls (49%, $p<0.001$). Most pronounced anesthesia avoidance was seen in 3-4-year-olds, with 55% of 3-4-year-olds able to avoid anesthesia, compared to 0-11% age-matched historical controls. Improvement in quality of life significantly increased during treatment for patients ages 5-7 years, and anxiety decreased throughout treatment for all age groups. AVATAR implementation is feasible across multiple institutions and should be further studied and made available to patients who may benefit from video-based distraction. Implementation and data collection

regarding the utility of a supportive care intervention among cooperating pediatric RT institutions is achievable in a large multicenter setting.

Figure Legends

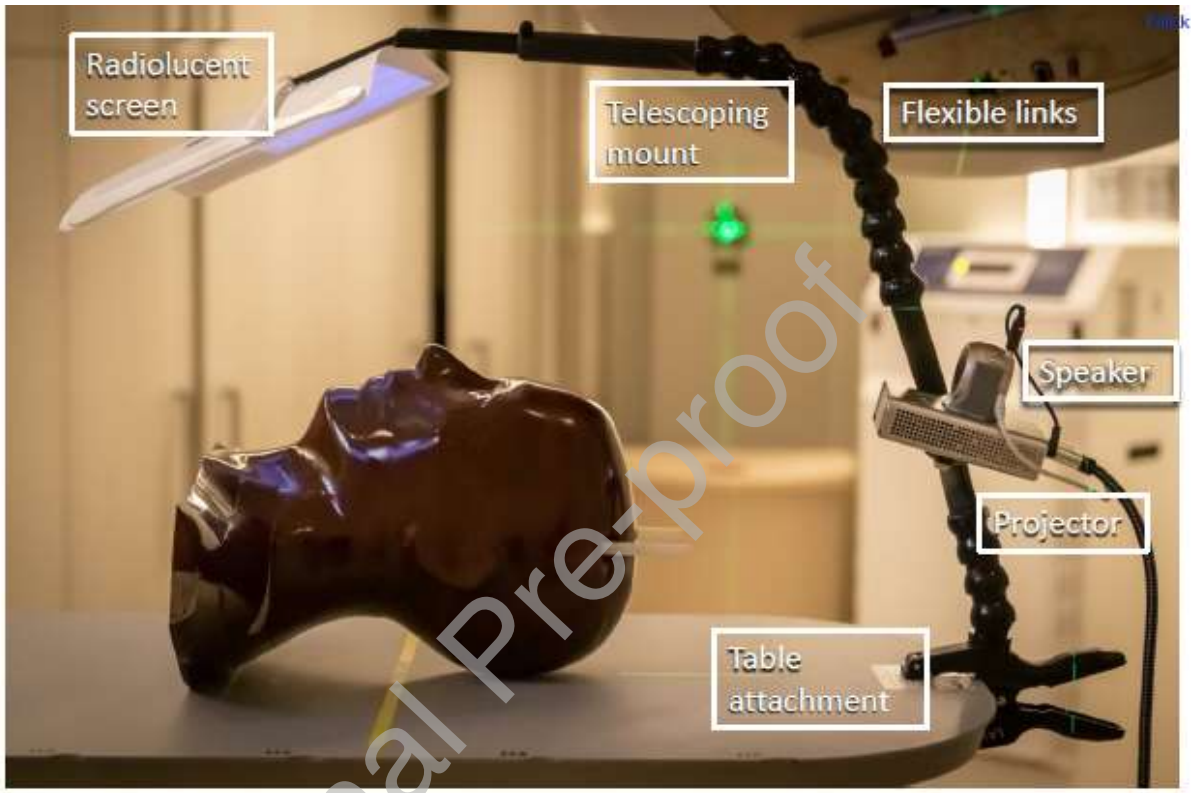

Figure 1. The AVATAR system, with radiolucent screen, telescoping mount, flexible links, projector with speaker, and treatment table attachment.

Figure 2. Anxiety scores, mYPAS, at baseline, midpoint, and end of treatment by age and treatment success.

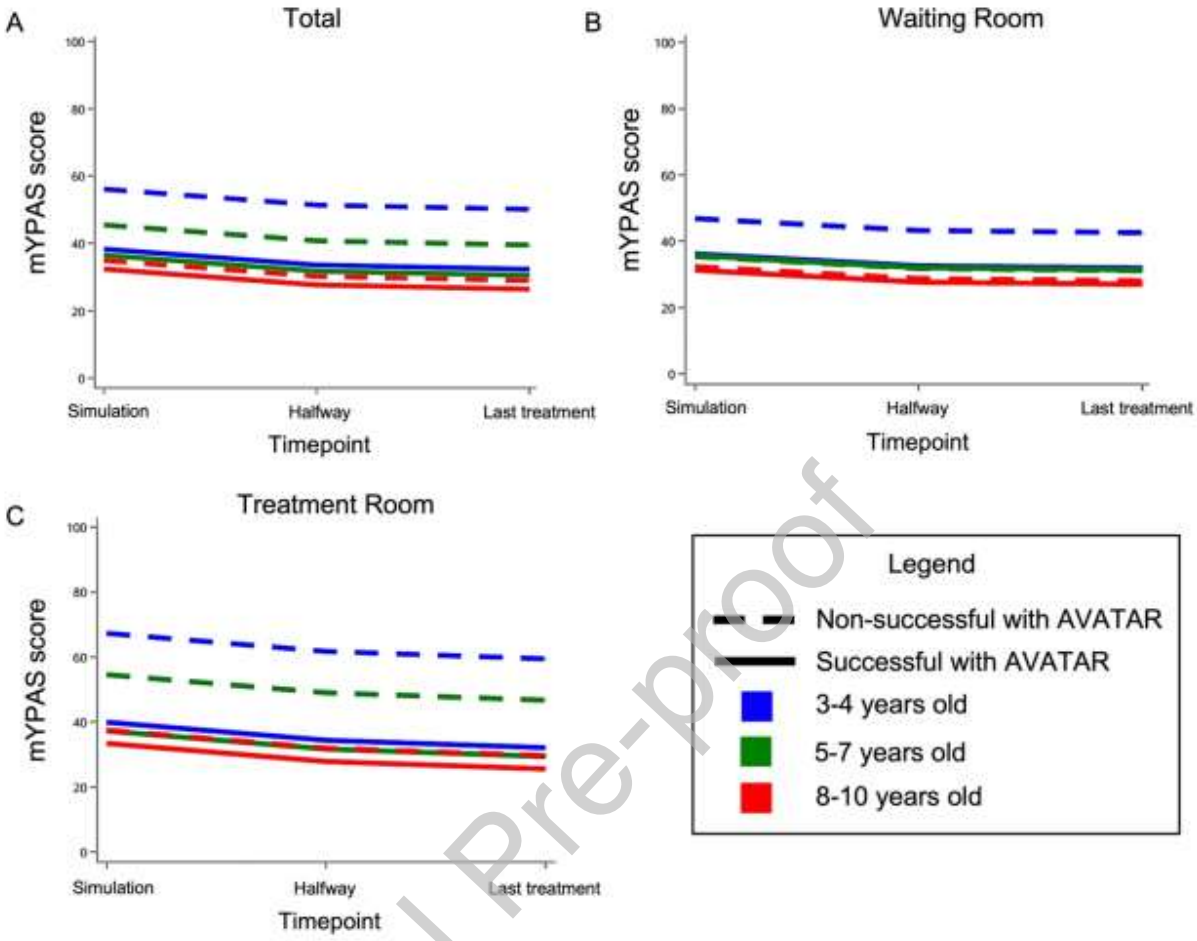

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Table 1. Patient demographic information

Characteristic	All (N=81)	Success (N= 63)	Non-success (N=18)	*P*
	N (%)			
Age				0.04
3-4	11 (13.6)	6 (54.5)	5 (45.5)	
5-7	36 (44.4)	29 (80.6)	7 (19.4)	
8-10	33 (40.7)	28 (84.8)	5 (15.2)	
Not reported	1 (1.2)	0 (0.0)	1 (100)	
Language				0.79
English	75 (92.6)	59 (78.7)	16 (21.3)	
Spanish	6 (7.4)	4 (66.7)	2 (33.3)	
Gender				0.78
Female	37 (45.7)	29 (78.4)	8 (21.6)	
Male	44 (54.3)	34 (77.3)	10 (22.7)	
Race				0.06
White	45 (55.6)	36 (80.0)	9 (20.0)	
Black/African American	11 (13.6)	8 (72.7)	3 (27.3)	
Asian	2 (2.5)	2 (100)	0 (0.0)	
American Indian/Alaska Native	1 (1.2)	1 (100)	0 (0.0)	
Unknown/not reported	22 (27.2)	16 (72.7)	6 (27.3)	
Health insurance				<0.001
Private	39 (48.1)	35 (89.7)	4 (10.3)	
Public	20 (24.7)	11 (55.0)	9 (45.0)	
Unknown/not reported	22 (27.2)	17 (77.3)	5 (22.7)	
Treatment site				0.85
Brain/spine	47 (58.0)	38 (80.9)	9 (19.1)	
Chest/abdomen	10 (12.3)	8 (80.0)	2 (20.0)	

Lung	5 (6.2)	4 (80.0)	1 (20.0)	
Total body	5 (6.2)	2 (40.0)	3 (60.0)	
Neck/jaw/maxilla	5 (6.2)	5 (100)	0 (0.0)	
Extremity	3 (3.7)	2 (66.7)	1 (33.3)	
Pelvis	3 (3.7)	2 (66.7)	1 (33.3)	
Orbit	2 (2.5)	2 (100)	0 (0.0)	
Unknown/not reported	1 (1.2)	0 (0.0)	1 (100)	
Treatment intent				0.98
Curative	34 (42.0)	26 (76.5)	8 (23.5)	
Palliative	11 (13.6)	8 (72.7)	3 (27.3)	
Not reported	36 (44.4)	29 (80.6)	7 (19.4)	

Table 2. Pediatric Quality of Life Patient mean scores

Quality of Life Category	Age category	Radiation Treatment Timepoint			P-value
		Simulation	Midpoint	Final	
Total scores	5-7	75.2	79.0	81.9	**0.008**
	8-10	77.9	79.9	79.7	0.52
Pain and Hurt	5-7	88.0	88.8	90.8	0.81
	8-10	78.9	81.0	74.4	0.58
Nausea	5-7	90.0	83.8	83.9	0.15
	8-10	83.5	84.7	80.6	0.56
Procedural Anxiety	5-7	40.3	43.9	47.1	0.17
	8-10	60.9	60.9	60.1	0.97
Treatment Anxiety	5-7	73.9	79.3	87.2	**0.01**
	8-10	79.5	86.0	89.6	**0.02**

Worry	5-7	76.4	85.1	83.8	0.24
	8-10	79.5	82.9	86.6	0.21
Cognitive Problems	5-7	75.7	84.2	82.3	0.16
	8-10	77.3	78.7	79.1	0.83
Perceived Physical Appearance	5-7	77.3	88.2	91.6	**0.001**
	8-10	85.5	88.3	90.3	0.13
Communication	5-7	76.8	77.7	87.8	0.09
	8-10*	---	---	---	---

- *Insufficient data for analysis*

Table 3. Pediatric Quality of Life, Guardian mean scores

Quality of Life Category	Age category	Radiation Treatment Timepoint			P-value
		Simulation	Midpoint	Final	
Total scores	3-4	78.3	85.6	81.5	0.79
	5-7	72.5	75.2	77.2	**0.006**
	8-10	78.2	79.2	79.7	0.76
Pain and Hurt	3-4	85.0	90.0	86.7	0.97
	5-7	76.8	80.8	84.6	**0.01**
	8-10	80.4	85.4	79.1	0.92
Nausea	3-4	80.7	89.3	91.3	0.24
	5-7	84.7	81.7	82.3	0.63
	8-10	83.5	86.3	81.6	0.85
Procedural Anxiety	3-4	48.9	67.8	60.0	0.42
	5-7	43.6	42.8	51.7	**0.04**
	8-10	58.6	54.8	61.6	0.78
Treatment	3-4	64.4	82.2	81.1	0.08

Anxiety	5-7	64.0	74.9	73.7	**0.04**
	8-10	**79.0**	78.9	82.3	0.74
Worry	3-4	93.3	96.7	81.7	0.27
	5-7	80.3	79.9	84.2	0.47
	8-10	84.5	80.4	85.4	0.98
Cognitive Problems	3-4	81.1	77.2	83.3	0.92
	5-7	78.8	79.0	76.5	0.68
	8-10*	---	---	---	
Perceived Physical Appearance	3-4	95.6	97.8	91.1	0.67
	5-7	80.6	83.1	83.2	0.67
	8-10	85.0	83.8	83.7	0.93
Communication	3-4	77.8	72.8	76.7	0.94
	5-7	71.8	76.1	79.8	0.10
	8-10	77.0	83.8	83.3	0.18

* *Insufficient data for analysis*