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TITLE: Hyperbaric Oxygen Therapy to Mitigate Childhood Radiation-Induced Neurocognitive and Skeletal Toxicity: Multimodality Evaluation in a Young Rodent Model

PRINCIPAL INVESTIGATOR: John Kalapurakal, MD

CONTRACTING ORGANIZATION: Northwestern University, Evanston, IL

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6. AUTHOR(S)
John Kalapurakal, MD (PI)
Craig Weiss, PhD (Co-I)

E-Mail:j-Kalapurakal@northwestern.edu

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Northwestern University
Department of
Radiation/Oncology
251 East Huron St.
Chicago, IL. 60611

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13. SUPPLEMENTARY NOTES

14. ABSTRACT
The purpose of this grant is to test the hypothesis that hyperbaric oxygen therapy (HBOT) can ameliorate or prevent the damaging effects of radiation therapy (RT) used to treat cancer in pediatric subjects. Effects of HBOT will be tested on the musculoskeletal (MSK)system and on cognitive abilities in mice. Hindlimbs are being assayed with CT and with physical measurements. The brain is being examined with multimodal imaging, assays for molecular biomarkers, neuropathological analyses, and multiple behavioral assays. Results thus far indicate the following: 1). Mice can tolerate HBOT (20 sessions: M-F, 90 min each for 4 weeks, 2 ATM) and hindlimb RT (20Gy, 1 fraction); 2). After 6 months of follow-up after RT there are no significant MSK changes. 3). On longer follow up we are beginning to see MSK changes, thus we will continue to follow the mice until we get to the primary end point of MSK injury. We will then be able to evaluate the protective effects of HBOT. 4). We have detected early RNA seq and serum cytokine biomarker expression after RT.

15. SUBJECT TERMS
Hyperbaric oxygen, radiation therapy, musculoskeletal, neurocognition, RNA-sequencing, serum biomarkers

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1. INTRODUCTION

This grant is designed to test the hypothesis that hyperbaric oxygen therapy (HBOT) may decrease the damaging effects of radiation therapy (RT) on neurocognitive functioning (NCF) and musculoskeletal growth (MSG) in children with cancer. We are using a pediatric-age matched mouse model treated with varying combinations of RT and HBOT in a randomized study, and we are utilizing a comprehensive advanced multi-modality diagnostic panel including neurocognitive, physical, advanced imaging, molecular, serum biomarker and pathology end points.
We started our work testing for musculoskeletal growth effects that will be followed by neurocognitive growth effects. We describe the specific aims and subtasks and results below.

2. KEYWORDS

Hyperbaric oxygen, radiation therapy, musculoskeletal, neurocognition, RNA-sequencing, serum biomarkers

3. ACCOMPLISHMENTS

STUDY TIMELINE	Year 1				Year 2				Year 3			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Regulatory Approval	X											
Aim1- Experiment Males Musculoskeletal tests	X	X	X	X								
Aim2- Experiment Males Neurocognitive tests				X	X	X	X					
Aim1- Experiment Females Musculoskeletal tests						X	X	X	X			
Aim2- Experiment Females Neurocognitive tests								X	X	X	X	
Data Analysis				X	X	X	X	X	X	X	X	X

SPECIFIC AIM 1: Determine the impact of HBOT on Neurocognitive functioning of pediatric age matched C57Bl6 mice following whole brain RT (10Gy in one fraction) utilizing a battery of neurocognitive tests in mice randomized to six treatment arms.

Percent completion: 0%

Detailed description of work: *The work on this Aim will begin in January 2024 after completion of the work in Aim 2 on December 30, 2023.*

SPECIFIC AIM 2: Determine the impact of HBOT on Skeletal development of pediatric age matched C57Bl6 mice following whole hind limb RT (20Gy in 1 fraction to entire one hind limb) utilizing physical and imaging measurements of limb length and diameter in mice randomized to six treatment arms.

Major Task: Determine the impact of HBOT on Musculoskeletal growth of pediatric age matched C57Bl6 mice following whole Limb RT (20 Gy in one fraction) utilizing physical and CT scan measurements and multimodality testing in mice randomized to six treatment arms.

Experiment Thirty pediatric age-matched mice of each gender were randomly assigned to six experimental arms (see table below) for a total of 180 male and 180 female mice.

TREATMENT ARMS	AIM 2 (MSK growth)
1. Control A	Room air in HBOT chamber
2. Control B	Pressurized air in HBOT chamber
3. RT	20Gy in one fraction to *one hind limb*
4. HBOT	20 sessions M-F, 90 min each, 2.0 ATM
5. RT→HBOT	RT 20Gy→HBOT (20 sessions M-F, 90 min each, 2.0 ATM) will start ***2 months*** later
6. HBOT→RT	HBOT (20 sessions M-F, 90 min each, 2.0 ATM) → RT 20Gy will be *given* ***1 month*** after HBOT

Detailed description of work:

Radiation therapy

The mice were anesthetized with ketamine/xylazine, placed in a holder with their left hindlimb extended and secured to a plastic block. The bodies, except for the left hindlimb, were shielded from radiation by placement of lead blocks. The irradiator is a Gammacell® 40 Exactor with a 137Cs source that has an average gamma ray energy of 660 keV and a central dose rate of 1Gy/min using standard RT procedures. The irradiator has a sensor to determine the required exposure time to deliver 20 Gy. A reversal agent for the xylazine was administered after the irradiation and the mice were placed back into their home-cage atop a warming pad until the mice were ambulatory. Mice were then returned to the vivarium.

Hyperbaric oxygen therapy (HBOT)

Mice were placed in the HBOT chamber and treatments were delivered with 100% oxygen at 2.0 atmosphere (ATM) pressure for 90 minutes daily, Monday through Friday. A total of 20 HBOT sessions were administered to the animals assigned to HBOT over 4 weeks. A 15-minute ramp up time was used to gradually increase the pressure from room air to 2.0 ATM, before the 90-minute treatment time was started. Likewise, a 15-minute depressurization time was used to gradually reduce the pressure in the HBOT chamber from 2.0 ATM to room air, after the 90-minute treatment. This practice is similar to human protocols and is done for the safety of the mice and prevent barotrauma injury to the ear drums, sinuses, bowels, and lungs. The HBOT chamber has in-built viewing mechanisms on the cover/lid through which the movements, activity, and safety of the mice were monitored by the technician every 15 minutes during HBOT treatments.

Hyperbaric air and Control groups

For the control groups, mice were placed in the HBOT chamber for 90 minutes in room air under normal pressure (Control A) and pressurized room air (Control B), respectively. The time interval between HBOT and RT in arms 5 and 6 are shown above.

RESULTS

SAFETY AND TOLERANCE OF RT AND HBOT

All 360 mice tolerated the RT and HBOT very well with no toxicity or mortality at any time during their follow-up until now **(Day 240 for male mice as of Mid-December 2023).**

Subtask 1: Physical measurements of musculoskeletal growth for all study arms for Aim 2 and both male and female genders, on days 30, 60, 90, 120 150 and 180, physical measurements will be made of treated and untreated limb using calipers of limb diameter at fixed points along the limb and total limb length.
RESULTS We have completed measurements for all male mice for all time points (see tables and figures below for mean weight, mean limb length and mean limb width of the irradiated (left side) limb for all treatment groups. Representative time points at Baseline (T1), 60 days (T2) and 180 days (T3) are shown. We continue to perform the same for the female mice.

Weight

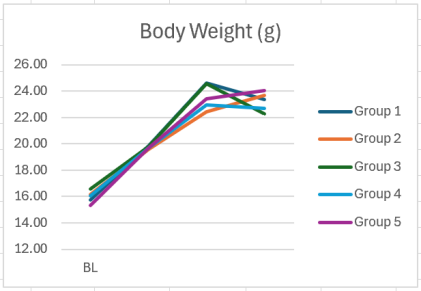
Group	BL	T1	T2	T3
1	15.73	19.83	24.63	23.39
2	16.13	19.56	22.42	23.67
3	16.55	19.80	24.55	22.28
4	16.03	19.70	22.93	22.67
5	15.33	19.67	23.42	24.03
6	15.58	18.90	23.20	22.20

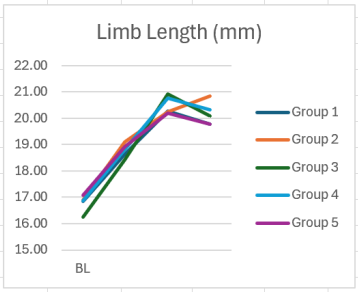
Limb Length

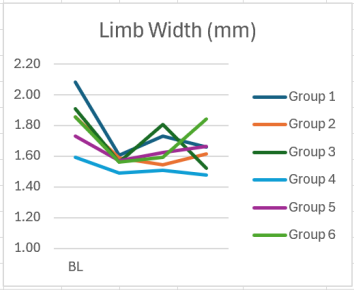
Group	BL	T1	T2	T3
1	16.84	18.65	20.28	19.78
2	16.91	19.09	20.25	20.84
3	16.24	18.44	20.93	20.08
4	16.87	18.82	20.77	20.32
5	17.08	18.92	20.19	19.78
6	16.76	19.09	20.69	19.86

Limb Width

Group	BL	T1	T2	T3
1	2.08	1.60	1.73	1.66
2	1.85	1.59	1.54	1.61
3	1.91	1.56	1.81	1.52
4	1.59	1.49	1.51	1.48
5	1.73	1.57	1.62	1.66
6	1.85	1.56	1.59	1.84







Percent completion: 100% for male mice, ~60% complete for female mice.

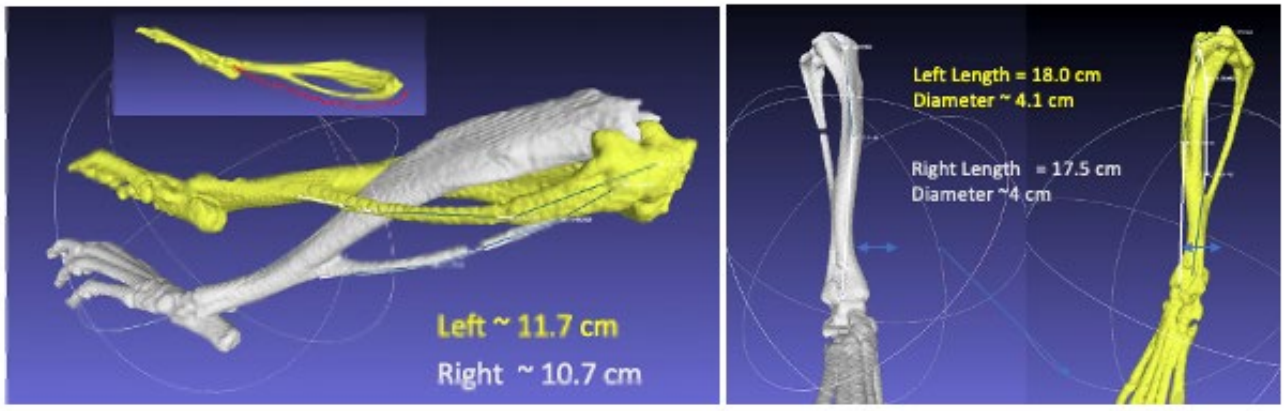
CONCLUSIONS

1. The RT and HBOT treatments were very well tolerated with no ACUTE toxicity or mortality.
2. At the 6-month (Day 180) time point we have NOT noticed any consistent or significant difference in limb dimensions in the irradiated limb using physical caliper measurements * (SEE BELOW FOR FURTHER FOLLOW-UP).

Subtask 2: Multimodal Imaging (MSK)
Percent completion: 100%*
Detailed description of work: Preclinical X-ray CT imaging was performed to obtain muscle-skeletal data including bone length and muscle alterations including bone density associated with treatment interventions. We stated in the protocol that 9 mice each from one control arm and four treatment arms (Aim 2) for male gender only, on Day 90 and 180. We have in fact imaged a group of mice from all cohorts at baseline, day 90 and day 180.

RESULTS

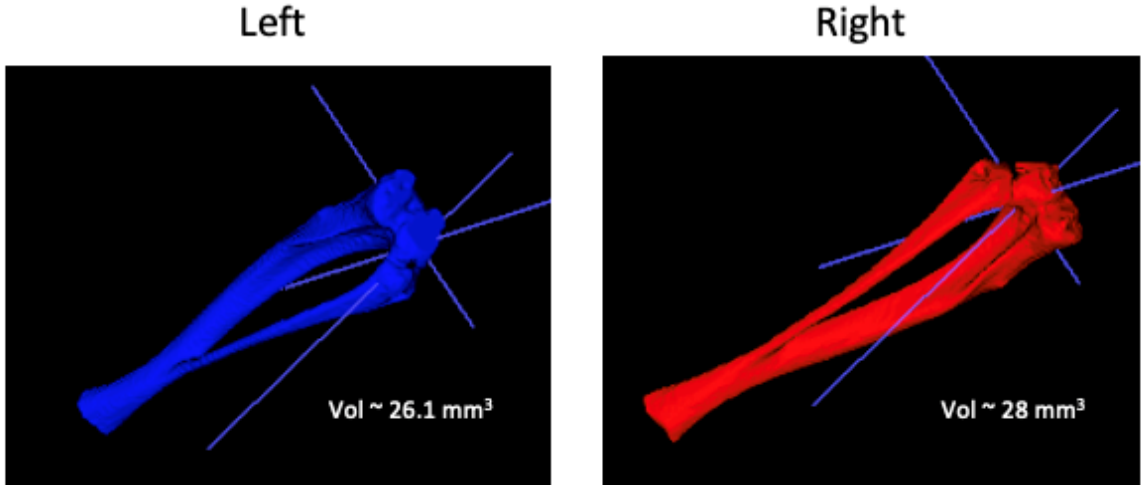
At 6 months follow-up (day 180) we see no differences in the bone length and bone density (femur, tibia) and muscle mass between the irradiated and control limbs in any of the treatment groups. See figure below of an example of one mouse at 6-month mark after RT using linear imaging.



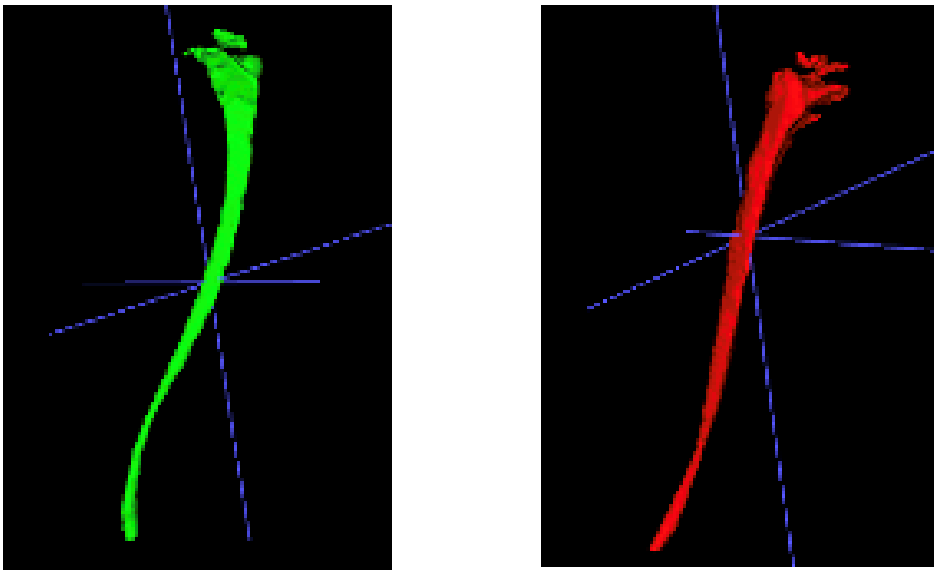
Conclusions: Our current experimental analysis suggests that linear measurements cannot provide a reliable and consistent biomarker unless radiation induced damages exceed a certain threshold that has not been reached currently. * SEE BELOW FOR FURTHER FOLLOW-UP.

FURTHER FOLLOW UP BEYOND DAY 180 TO ESTABLISH THE CONSISTENT EFFECTS OF RT SO AS TO THEN STUDY THE MITIGATING EFFECTS OF HBOT

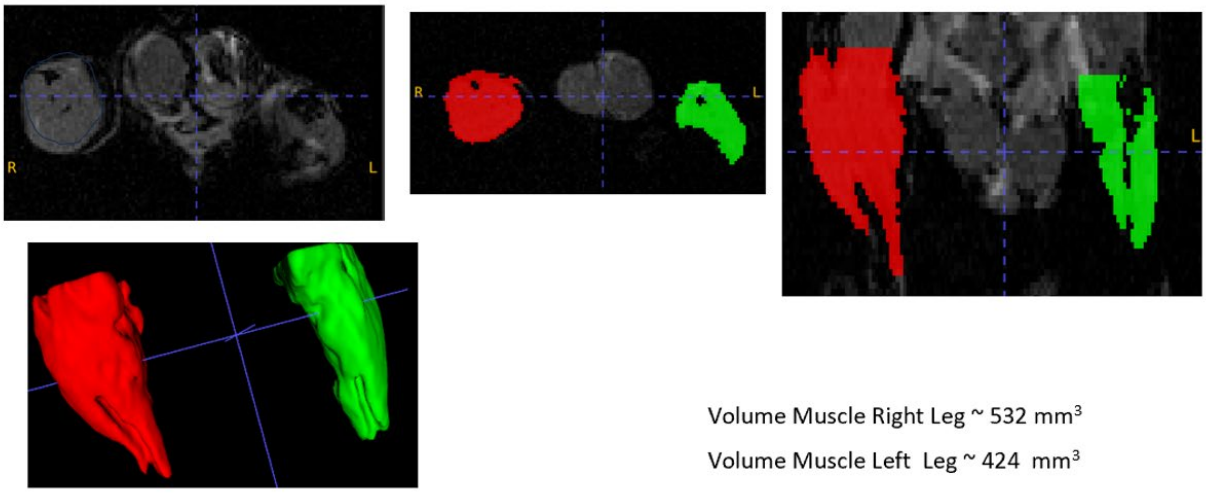
Given the lack of consistent RT induced injury in the radiated limb in our cohort of male mice, we decided to continue follow-up of these mice beyond 6 months until we see late RT effects consistently and to then be able to evaluate the mitigating effects of HBOT. As of now (December 2023), we have reached day 240 on the first batch of mice. We are beginning to notice limb thinning (loss of muscle mass) in the irradiated limb in approximately a third of mice in the RT-arm (Arm 3). Further, we performed additional more advanced imaging on a cohort of these mice that showed RT effects. We looked at a combination of regional morphological volumetrics focusing on specific skeletal regions (i.e., tibia). We were able to observe a radiation-induced growth retardation using this technique (see below).



To advance our ability further, we also quantified the size and volume of regional bone marrow canal driven by the knowledge that radiation can affect bone marrow tissue and ultimately induce progressive fibrotic growth which can lead measured decrease in bone marrow space volume. Representative comparison of left and right bone marrow canal is shown as rendered 3D images depicting the differences following radiation on day 240 is shown below.



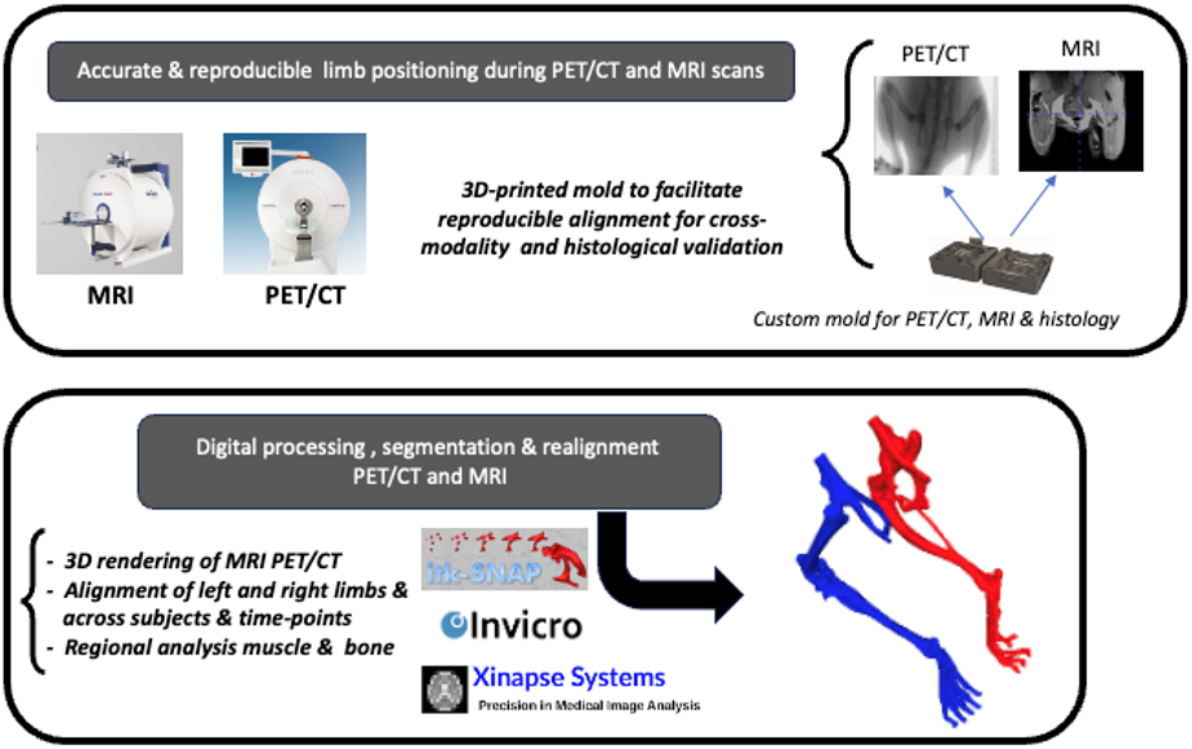
While the digital approach focusing on volumetric analysis of 3D data sets seems to provide some significant result in some irradiated mice at later time points beyond day 180, we feel that we need to develop a more robust tool to quantitatively measure with sufficient sensitivity and specificity to detect the therapeutic effects of RT and toxicity-mitigating effects of HBOT. For this reason, we have tested and are developing a multimodal imaging pipeline that involves integrating the soft-tissue data from MRI with that obtained from CT (for both muscle and skeleton). A representative example of a mouse showing atrophy (20% reduction in muscle mass in the radiated limb) utilizing both MRI and CT is shown below.



Volume Muscle Right Leg ~ 532 mm^3

Volume Muscle Left Leg ~ 424 mm^3

Thus, our current effort is being devoted to implement a processing pipeline involving several advanced image processing steps using both custom and commercial image processing tools included in different software packages (VivoQuant, ITK-SNAP, Jim7.0). Our progress and ongoing experimental pipeline are schematically depicted below. The expectation is to identify with longer follow-up the most relevant set of multi-imaging parametric data which can drive our assessment of RT and HBOT effects.



Specific Aim 3: Determine the impact of HBOT on serum biomarkers of inflammation.

Detailed description of work We will test 5 mice each from one control arm and four treatment arms (Aim 1 and 2) for male gender only, on Day 180, N=2, see below.

Percent completion: 0%, **because we have NOT consistently observed RT-injury in all irradiated mice, we have not performed the final sacrifice OF ALL MICE that was originally designated for day 180.**

However, we have been sacrificing 3 mice from each arm at intervals of 1-2 months and their tissues are being stored for future analysis per the protocol listed below.

Animals were placed under isoflurane anesthesia. A thoracotomy was performed to expose the heart and induce euthanasia. Blood samples were collected from the apex of the heart via insertion of a needle attached to a 1 mL syringe. Tissues and organs were collected in similar fashion for all animals for future histology evaluation, RNA/DNA sequencing, single cell RNA-seq and spatial gene expression analysis. Tissue and organs collected were limbs (radiated left and non-

radiated right limbs), heart, lungs, liver, spleen, brain, kidneys, and testes (for male mice). Half of the organs were snap frozen and the other half fixed. For formalin fixed tissues, one organ piece was placed into one cassette. All cassettes for each animal were placed into a single 240-mL specimen cup filled with 10% neutral buffered formalin at room temperature. For snap-frozen tissues, one organ piece was placed into an empty RNase-free cryovial, then vial was immediately dropped into liquid nitrogen.

Blood collection: Animals were placed under isoflurane anesthesia. A thoracotomy was performed to expose the heart and induce euthanasia. Blood samples were collected from the apex of the heart via insertion of a needle attached to a 1 mL syringe. Blood samples were aliquoted into two portions:

For RNA-seq analysis, mice blood samples were placed into K_2-EDTA microfuge tubes and placed on wet ice. RNA was extracted from these samples and RNA-seq was performed to determine gene expression changes.

For cytokine analysis, the collected blood sample from female mice was placed into an empty microcentrifuge tube placed on indirect wet ice. The blood was allowed to clot for 20-30 minutes prior to centrifugation (1,000 x *g* for 10 minutes at 20-25°C). Serum was collected from the top separated fraction using a pipette and was stored at -80°C for future cytokine analysis.

PRELIMINARY RESULTS

To standardize procedures of RNA seq and cytokine analyses at the end point of our experiment, our laboratory investigators performed RNA seq on blood and cytokine analysis on serum in a cohort of animals sacrificed at earlier time points. No DOD funds were utilized for this work. The results are summarized below.

For the RNA-seq, a total of 6 samples were used with 3 from the control and another 3, 24 hours after RT. Differential gene expression analysis yielded a total of 1,016 genes that have significant differences in expression between the control group and the radiation group. Of these significantly differentially expressed genes, 721 were upregulated in radiation compared to control while 295 were downregulated in radiation. Biological pathway analysis was performed on these gene lists to identify possible pathways that might be affected by radiation exposure. The results demonstrate possible pathways among the upregulated genes include: 1) Signaling by Rho GTPase, 2) Neutrophil degranulation, and 3) Adaptive immune system. Leukocyte differentiation was among the pathways significantly associated with the downregulated genes.

ThermoFischer ProcartaPlex multiplex (PPX) immunoassays and Luminex xMAP (multi-analyte profiling) technology were used to assay cytokines. Luminex technology uses differently dyed capture beads for each target in a multiplex ELISA-like assay enabling simultaneous analysis of multiple cytokines in a single sample of serum. We selected a PPX with 36 analyte proteins (either for pro-inflammatory or adaptive immunity cytokines) which are specifically expressed in an immune response post trauma, i.e., post-radiation therapy. Serum samples were collected at 6 hours, 24 hours, and 1-week post RT and were evaluated in duplicate (2 x 25 ul). The analysis was performed in two runs with the 24-hour samples followed by the 6 hour and 1-week samples.

Out of 36 cytokines evaluated, 16 cytokines were detected in at least 1 out of 3 animals from each group. Of the detected cytokines, 7 were consistently present (at least 2/3 animals per group). These cytokines were: ENA-78, Eotaxin, GM-CSF, GRO alpha, IL-12p70, IP-10, and MCP-3.

Using the GraphPad software, we performed multiple comparison analysis followed by Tukey's multiple comparisons test. The analysis demonstrated significant increase ($P < 0.05$) of the following cytokines in the RT-1wk group compared with the control air-24h group:

- Interferon gamma inducible protein-10 (IP –10) - control air- 24h: 20.15±2.08 vs. RT-1wk: 28.53±2.05
- Chemokine growth-regulated protein alpha GRO-α- control air- 24h: 8.60±0.16 vs. RT-1wk: 19.11±1.00
- Epithelial neutrophil-activating peptide (ENA-78) - control air- 24h: 88.12±33.56 vs. RT-1wk: 188.2±29.72

From the 7 biomarkers listed above, 3 cytokines were consistently present (2-3/3 animals per group) in the 6h-post acute radiation group. These cytokines were: G-CSF, IL2, and IL22). G-CSF is a potent stimulator of hematopoietic mobilization in response to inflammatory stimuli and plays a pivotal role in the expansion and differentiation of neutrophils in the bone marrow and their subsequent release into the blood circulation. IL-2 has an immunoregulator targeting activated T, B, and NK cells and hence has an immuno-adaptive role. IL-22 is a pro- and anti-inflammatory cytokine that is mainly produced by T cells and NK cells.

There were 6 cytokines that were present inconsistently (only 1-3 animals per group). They were LIF, IL-1beta, IL-9, IL-23, IFN-gamma, and MIP-1 alpha.

Cytokines - Not Detected (0/3 animals per group)		Cytokines - Detected (1-3/3 animals per group)		Cytokines Common to All Groups (2/3 animals per group)		Cytokines detected mostly in 6h-post RT (2-3/3 animals per group)	
1	IFN alpha	1	ENA-78	1	ENA-78	1	G-CSF (3/3)
2	IL-1 alpha	2	Eotaxin	2	Eotaxin	2	IL-2 (2/3)
3	IL-10	3	G-CSF	3	GM-CSF	3	IL-22 (3/3)
4	IL-13	4	GM-CSF	4	GRO alpha		
5	IL-15	5	GRO alpha	5	IL-12p70		
6	IL-17A	6	IFN gamma	6	IP-10		
7	IL-18	7	IL-1 beta	7	MCP-3		
8	IL-27	8	IL-12p70				
9	IL-28	9	IL-2				
10	IL-3	10	IL-22				
11	IL-31	11	IL-23				
12	IL-4	12	IL-9				
13	IL-5	13	IP-10				
14	IL-6	14	LIF				
15	MCP-1	15	MCP-3				
16	M-CSF	16	MIP-1 alpha				
17	MIP-1 beta						
18	MIP-2 alpha						
19	RANTES						
20	TNF alpha						

What were the major goals of the project?
Please see above.

What was accomplished under these goals?
Please see above.

What opportunities for training and professional development has the project provided?

Nothing to Report.

How were the results disseminated to communities of interest?

Nothing to Report.

What do you plan to do during the next reporting period to accomplish the goals?

During the next reporting period we will provide data after longer follow up of mice treated in MSK experiment. We will also provide early results from brain RT/HBOT and neurocognitive functioning.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

The results of this study may provide a treatment, HBOT, to mitigate RT damage to the brain and musculoskeletal tissues in children with cancer. Presently there are no treatments for this condition.

What was the impact on other disciplines?

Nothing to Report.

What was the impact on technology transfer?

Nothing to Report.

What was the impact on society beyond science and technology?

Radiation therapy (RT) is an integral component of the multimodality management of most pediatric cancers. However, it is also the most common cause of toxicity in childhood cancer survivors (CCS). The effects of RT result in somnolence, lethargy, intellectual disabilities and brain necrosis. The neurologic toxicity especially impaired neurocognitive function (NCF), including memory and emotional functioning, and is a devastating toxicity that significantly impacts all aspects of life and social functioning of CCS. Secondary malignant tumor induction is another severe late toxicity of RT on the CNS. The effects of RT on the skeletal system include decreased vascularity, reduction of bone cells and chondrocytes thus impairing and arresting chondrocyte and bone cell proliferation, retarding bone growth and remodeling. Further, RT causes collagen denaturation leading to impaired mineralization and reduction in mechanical properties such as bone stiffness and flexural strength. The damaging effects of RT on the musculoskeletal system (MSK) following treatment of pediatric solid tumors like sarcomas, neuroblastoma and Wilms tumor can result in significant growth deformities and fractures. All of these RT-induced toxicities significantly and adversely impact the quality of life, and the physical, emotional, psychosocial and long-term health of childhood cancer survivors and their families. The use of HBOT to mitigate RT induced damage will greatly impact the survival and quality of life of childhood cancer survivors and thus provide a major contribution to society.

5.CHANGES/PROBLEMS:

We implemented one minor change from the initial plan, i.e., we started the project by looking at effects on the musculoskeletal system (Aim 2) first.

Problems:

1). We had difficulty hiring staff after the COVID pandemic and hence there was an initial delay in starting the work.
2). At day 180 following RT, we have NOT observed consistent signs of RT injury. However, after 8 months of follow up, we have begun to notice late signs of RT injury. We will thus monitor these mice for another 4- 6 months until we reach the end point for this study.

Changes in approach and reasons for change

As stated above, we flipped the order of Aims 1 and 2. We realized that we would be able to test the effectiveness of HBOT much more quickly during Aim 2 than during Aim 1. The results of Aim 2 would inform us about the safety and effectiveness of the treatments when used during Aim 1.
As stated above, we have postponed the final sacrifice of animals from day 180 (6 months) to at time point at which we have observed consistent signs (physical and imaging) of RT injury in all mice after RT. Only then will we be able to evaluate the mitigating effects of HBOT in this experiment.

Actual or anticipated problems or delays and actions or plans to resolve them.

Please read above statements.

Changes that had a significant impact on expenditures

Our pilot data were collected with a small older model hyperbaric chamber. We purchased (at our own expense, about $60k) a commercially available hyperbaric chamber used by veterinarians which enables us to use more mice simultaneously, with better visibility of the mice, and with easier and better control of the gas pressure. Similarly, we had the University install a custom gas manifold that enables us to switch between air and oxygen safely and easily. These changes reduced the amount of gas used for the experiments and the time required to complete treatments.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents.

None

Significant changes in use or care of human subjects

Not applicable.

Significant changes in use or care of vertebrate animals

Northwestern University IACUC approval was granted on 4/21/2022.
ACURO protocol CA210275.e001 was granted on 8/22/2022.

Significant changes in use of biohazards and/or select agents.

Nothing to Report.

6. PRODUCTS:

Nothing to Report.

- **Publications, conference papers, and presentations**

Report only the major publication(s) resulting from the work under this award.

Nothing to Report.

Journal publications.

Nothing to Report.

Books or other non-periodical, one-time publications.

Nothing to Report.

Other publications, conference papers and presentations.

Nothing to Report.

- **Website(s) or other Internet site(s)**

Nothing to Report.

- **Technologies or techniques**

We have added multimodality imaging techniques such as MRI and 3D volume analysis as stated above.

- **Inventions, patent applications, and/or licenses**

Nothing to Report.

- **Other Products**

Nothing to Report.

7.PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Name: John Kalapurakal, MD
Project Role: PI
ORCID Identifier:
Person month worked: 0.84
Contribution to Project: Director of project.
Funding Support:

Name: Daniel Jay Brat
Project Role: Co-I
ORCID Identifier:
Person month worked: 0.6
Contribution to Project: Pathology (Chair of Department)
Funding Support:

Name: Craig Weiss, PhD
Project Role: Co-I, IACUC PI
ORCID Identifier: 0000-0002-9861-8727
Person month worked: 1.2
Contribution to Project: Director of Behavioral Phenotyping Core, established IACUC protocol, determined space for HBOT and behavioral assays.
Funding Support:

Name: Daniele Procissi, PhD
Project Role: Co-I, Director of Imaging facility
ORCID Identifier:
Person month worked: 0.6
Contribution to Project: Director of MRI facility
Funding Support:

Name: Monalisa Navarre
Project Role: Co-I
ORCID Identifier:
Person month worked: 12
Contribution to Project: Maintains mouse colony, collects data,
Funding Support:

Name: Rizaldi Scott
Project Role: Co-I, Director, Neuropathology Core
ORCID Identifier:
Person month worked: 0.6
Contribution to Project: Prepares and analyzes tissue for detection of pathology.
Funding Support:

Name: Xinkun Wang
Project Role: Co-I, Director NUSeq Core
ORCID Identifier: 0000-0003-1377-0509
Person month worked: 0.6
Contribution to Project: Analyzes DNA and RNA from mouse tissues.
Funding Support:

Name: Nayereh Ghoreishi-Haack
Project Role: Co-I, Director Developmental Therapeutics Core
ORCID Identifier: 0000-0001-9660-595X
Person month worked: 0.48
Contribution to Project: Collects and prepares blood and tissue samples for Pathology and NUSeq cores.
Funding Support:

Name: Ruohui Chen

Project Role: Co-I
ORCID Identifier:
Person month worked: 0.6

Contribution to Project: Statistician
Funding Support:

Name: Serpil Kucuker Dogan
Project Role: Co-I
ORCID Identifier:
Person month worked: 0.06
Contribution to Project: Radiation physicist
Funding Support:

Name: Mahesh Gopalakrishnan M.S.,
Project Role: Consultant
ORCID Identifier:
Person month worked:
Contribution to Project: Senior radiation physicist
Funding Support:

Name: Claude Zanetti, MD
Project Role: Consultant
ORCID Identifier:
Person month worked:
Contribution to Project: Use of HBOT facility
Funding Support:

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report.

What other organizations were involved as partners?

Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: Not Applicable

QUAD CHARTS: Not Applicable

9.APPENDICES: *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*

Not applicable