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LEGACY HEALTH OFFICE OF PHILANTHROPY
FY19 RESEARCH GRANT APPLICATION FORM

Requestor name: Leslie Sorenson — **Title:** Manager, Oncology Research

*Enoch Huang, MD — Director, Legacy Hyperbaric Medicine

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Department: Oncology Research — **Facility Code:** 200 **Cost Center:** 3540

Hyperbaric Medicine — **Facility Code**: 700-3540

Program/Project Title (30 characters max): A pilot study comparing acute post-radiation hyperbaric oxygen (HBO_2) versus Trental and Vitamin E for breast cancer patients who have recently completed radiation therapy as part of their treatment course.

(If previously funded, please reference prior grant name in title.)

X New Program/Project

☐ Previously Funded Program/Project *(You must also submit a Research Grant Progress Report.)*

Which Site(s) will patients be from:	**To What Extent?**
(Indicate which site(s) patients enrolled in the study are from. Please check appropriate boxes and then estimate % of patients by site.)	
☐ Randall Children's Hospital	_____
X Emanuel Medical Center	5
X Good Samaritan/Oncology Research	80
X Meridian Park Medical Center	5
X Mount Hood Medical Center	5
X Salmon Creek Medical Center	5
☐ Silverton Medical Center	_____
☐ Legacy Hospice	_____
☐ Unity Center for Behavioral Health	_____

Please respond to the following questions in no more than 5 pages.

1. **In layperson's terms, please provide a brief abstract of the proposed project** (1 paragraph max):

Legacy oncology clinical research, in collaboration with Legacy Health Hyperbaric Medicine, have been working to develop a pilot study comparing acute post-radiation hyperbaric oxygen (HBO_2) versus Trental and Vitamin E for breast cancer patients who have recently completed radiation therapy as part of their treatment course. Patients who have been treated with radiation therapy often develop collateral tissue injury, resulting in hypocellular, hypovascular, and hypoxic tissues. This tissue is at increased risk of fibrosis, infection, ulceration, and poor healing of wounds. These symptoms commonly show up 6 months or more after completion of radiation therapy, and it is difficulty to identify patients who will develop complications versus those that will not.

2. What is the specific clinical relevance of your proposal?

Hyperbaric oxygen therapy is an approved treatment modality for delayed radiation treatment injury, stimulating angiogenesis in irradiated tissue and improving capillary density and reducing morbidity. There is preliminary data that shows that acute post-operative HBO_2 improves quality of life in patients who have had post-mastectomy radiation therapy. Legacy oncology clinical research conducted/completed/published in 2016 a pilot study funded by the Legacy Foundation. The study demonstrated that a 6-month course of pentoxifylline and Vitamin E was able to successfully improve quality of life in this patient population. We wish to compare patients that receive hyperbaric oxygen *or* pentoxifylline and Vitamin D immediately after completion of radiation therapy.

3. Please describe the specific aims of the study:

Patients would be pre-screened, consented and enrolled in the study before completion of radiation therapy treatment. Baseline assessments include QOL questionnaires, surgical complications and tissue quality visual assessments would happen during this visit.

Study subjects will receive one of two active treatments:

- Pentoxifylline (400 mg, three times daily) plus Vitamin E (400 IU, twice daily) x 6 months
- 100% oxygen at 2.2 atmospheres absolute, 90 minutes, Monday-Friday for 30 sessions (6 weeks)

A third, control group will consist of patients who have not received either of the two active treatments. This will allow us to demonstrate whether one, or both, treatment is superior to the current standard of care. This control group would come from our current cancer registry population of patients with the same cancer history and who have received radiation therapy as part of their treatment course.

We will collect both objective and subjective measures to determine efficacy of treatments at multiple time points:

- Upon successful enrollment into the study and prior to randomization
- Immediately upon completion of the 6 weeks of hyperbaric exposure
- 3 months after completion of hyperbaric exposure
- After completion of oral tablets (6 months after enrollment)
- 1 year, 3 years and 5 years after enrollment

<u>Subjective</u>

- Quality of Life survey (SF-12)
- Reduction of breast fibrosis Visual Analog Scale

<u>Objective</u>

- Incidence of delayed wound healing, surgical complications, implant revision or loss
- Baker's grade assessment
- Tissue compliance using a tissue compliance meter

The proposal would be to enroll approximately 30 patients in each active arm the study, although we will consult with a biostatistician to calculate the number of patients to show adequate power to demonstrate a real effect.

4. As succinctly as possible, please describe other relevant studies and how this study builds on that work?

Most studies have focused on hyperbaric oxygen treatment for late effects radiation-induced tissue toxicity (6 months or greater), but recent studies by Teguh have suggested that earlier hyperbaric oxygen therapy immediately after radiation could have downstream benefits. Patients in our study would start study related treatments within 2 days of completing radiation therapy

The first reference is from Legacy Health and was able to be completed thanks to the gracious support of our foundation.

Am J Surg. 2016 May;211(5):854-9. doi: 10.1016/j.amjsurg.2016.01.006. Epub 2016 Feb 22.
Prophylactic use of pentoxifylline (Trental) and vitamin E to prevent capsular contracture after implant reconstruction in patients requiring adjuvant radiation.
Cook M[1], Johnson N[2], Zegzula HD[3], Schray M[4], Glissmeyer M[5], Sorenson L[6].

Radiat Oncol. 2016; 11: 130
Hyperbaric oxygen therapy for late radiation-induced tissue toxicity: prospectively patient-reported outcome measures in breast cancer patients David N. Teguh

International Journal of Radiation Oncology*Biology*Physics Volume 75, Issue 3, 1 November 2009, Pages 711–716
Early Hyperbaric Oxygen Therapy for Reducing Radiotherapy Side Effects: Early Results of a Randomized Trial in Oropharyngeal and Nasopharyngeal Cancer David N. Teguh, M.D.

5. As succinctly as possible (no more than 1 page), describe your specific procedures and methods, including data collection and analysis.

Patients would be pre-screened, consented and enrolled in the study before completion of radiation therapy treatment. Baseline assessments include QOL questionnaires, surgical complications and tissue quality visual assessments that would happen during this visit.

We will collect both objective and subjective measures to determine efficacy of treatments at multiple time points:

- Upon successful enrollment into the study and prior to randomization
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Subjective

- Quality of Life survey (SF-12)
  Reduction of breast fibrosis Visual Analog Scale

Objective

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- Baker's grade assessment
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6. Timeframe: How long will this work take to complete and what are the key milestones or benchmarks?

Estimated annual expenses

It is estimated that we will enroll 10 patients in each arm per year, taking 3 years to complete the study. This would result in the following breakdown of costs: TOTAL of 60 patients

Finalize protocol and submit to the IRB within 2 months of approval from Legacy Foundation
Enrollment will commence within 2 weeks of IRB approval
Interim analysis after first 10 patients are enrolled in each arm to review study processes and benchmarks
Year 1 IRB Preparation, biostatistician support
(enroll 20 patients) 10 in each arm
Year 2 (enroll 20 patients) 10 in each arm
Year 3 (enroll 20 patients) 10 in each arm Biostatistician review and publication

7. Collaborators: please list all individuals who will collaborate or consult in your study.

Legacy Emanuel Hyperbaric Medicine Departments
Legacy Oncology Clinical Research * staff support all Legacy sites including OHSU cancer collaborative infusion sites.
Legacy Medical Group Surgical Oncology
Legacy Health Radiation Oncology
Legacy Cancer Institute

8. Describe specifically how foundation funds will be used. If other sources of revenue exist, please list source and amount:

Regulatory submission support
Biostatistician support
Coordinator time at limited time points
Purchasing and dispensing of study drugs
There will be no costs incurred by the hyperbaric oxygen treatments as the study patients will be treated concurrently with regularly scheduled patients. Any incidental costs (e.g., oxygen hood, oxygen tubing, staff time) will be absorbed by the hyperbaric department

9. If your application is funded, how will the results of this study be used to leverage other grants or support?

If the initial pilot study shows success we would like to expand the study to other cancer patients who have been treated with radiation therapy and develop collateral tissue injury. We would also approach the NIH and NCI for grant support as this has the potential to affect millions of patients who receive radiation every year.

10. Project Budget:

What is the total funding requested to complete this study: $15,822.00

If multi-year study, what is the annual amount needed in each of these years?
FY19 (April 1, 2018-March 31, 2019) $5442.00
FY20 (April 1, 2019-March 31, 2020) $3542.00
FY21 (April 1, 2020-March 31, 2021) $5342.00

Please attach a detailed budget using the FY19 Research Grant Budget Request Form