(i.e autoanitbody profile and internal organ involvement) and its impact on survival. METHODS/STUDY POPULATION: We measured serum E2 levels in 83 dcSSc men >50 years old from the University of Pittsburgh Scleroderma Center and healthy controls of similar age. Using statistical modeling, we examined the associations between circulating E2 levels, internal organ involvement, autoantibody profiles, and survival. RESULTS/ANTICIPATED RESULTS: Male dcSSc patients had significantly higher serum E2 levels compared to healthy male controls and compared to dcSSc post-menopausal women of similar age. Male dcSSc patients with high serum E2 levels had significantly more heart involvement and worse survival. Using Cox regression modeling for risk of death, increasing serum E2 levels in anti-Scl-70 antibody positive dcSSc males were associated an increased risk of death. DISCUSSION/SIGNIFICANCE OF IMPACT: DcSSc male patients have higher levels of E2 compared to healthy controls and dcSSc postmenopausal women. Elevated serum E2 levels in dcSSc males >50 are associated with heart involvement and, if anti-Scl-70 antibody positive, worse survival. Our current study expands on our previous work, not only that that E2 exerts pro-fibrotic effects on skin, but also internal organ involvement, overall survival. These data suggest an important role of estrogen imbalance in SSc.

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Fluorescence-Guided Neurosurgery with 5-Aminolevulinic-Acid and Second-Window-Indocyanine-Green: A murine model and investigation into suitable cell lines.

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OBJECTIVES/SPECIFIC AIMS: This study aims to understand the utility of 5-ALA and SWIG in detecting areas of neoplasm in a murine model of GBM. Primary outcome is the distribution of the two dyes in comparison to the true tumor extent; the sensitivity, specificity, PPV, and NPV of both dyes will be calculated. The secondary outcome is the suitability of existing cell-lines used for GBM research for studies in fluorescence-guided surgery. METHODS/STUDY POPULATION: Two cell lines are used for this research: U87, derived from human GBM; and GL261, derived from rodent stem cells. U87 are implanted intracranially into 6-week old athymic, nude, female mice, while GL261 are implanted intracranially into 10-week old female C57BL/6 mice. The mice are weighed every 3 days to monitor health and bioluminescence imaging is performed between 7-10 days after implantation to confirm tumor implantation and monitor tumor growth. The mice are sacrificed between 10-21 days after implantation. 5mg/kg of intravenous ICG is administered 24-hours prior to harvest and 250mg/kg of intraperitoneal 5-ALA is administered 3-hours prior to harvest. Once the mice are sacrificed, their brains are quickly harvested and placed in cold formalin. Using a high-resolution Odyssey CLx scanner, near-infrared fluorescence from ICG is captured in coronal cross sections of the brains through the tumor. Similarly, 5-ALA fluorescence is imaged using a 405nm LED excitation source and 610-690nm bandpass filter. Afterwards, slices of the brain are stained with H&E, which serves as the gold-standard of the extent of tumor. Images from ICG, 5-ALA, and H&E can then be compared using ImageJ to compare the extent of tumor to the distribution of the dyes. RESULTS/ANTICIPATED RESULTS: In separate, previous studies in humans, both 5-ALA and SWIG have demonstrated utility in detecting residual neoplasm in HGG resections. In general, 5-ALA is more specific for areas of neoplasm, while SWIG is more sensitive. Thus, I anticipate that in this study, SWIG will show a greater distribution than 5-ALA, with SWIG distributing to areas beyond the tumor and 5-ALA distributing within, but not completely covering, the tumor. SWIG's sensitivity and NPV for detecting tumor should be >90%, while its specificity and PPV may be closer to 50%. For 5-ALA, specificity and PPV should be close to 80-90%, but its sensitivity and NPV may be <50%. In terms of cell-line, preliminary results suggest that U87 cells are not suitable for research involving 5-ALA. We suspect that this is partly due to the limited infiltrative nature of U87 cells; in fact, the cells form a spherical mass, imitating metastases rather than true HGGs. The U87 masses do not have significant vascularity, which likely limits the amount of 5-ALA that can distribute to inside the tumor. DISCUSSION/SIGNIFICANCE OF IMPACT: 5-ALA is currently the only FDA-approved agent for fluorescence-guided neurosurgery. However, it has multiple limitations, which ultimately results in its low sensitivity and NPV. Our novel technique, which has demonstrated much higher sensitivity at the cost of specificity, offers an alternative that may help surgeons better achieve total resections in the operating room. These two agents have not been compared directly in humans or mice. Thus, this experiment sets up an important precedent, on which a human clinical trial comparing the two agents' effects on resection rates and patient outcome can be performed. Ultimately, this work will lay the foundation for future research into fluorescence-guided neurosurgery, both in the visible and NIR spectrum.

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Fracture Targeted Parathyroid Hormone Agonist As An Effective Pharmaceutical For Bone Repair in Mouse and Canine Models

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OBJECTIVES/SPECIFIC AIMS: The primary objective of this study was to evaluate the performance of a bone fracture targeted systemically administrable bone anabolic as a potential therapeutic for bone fracture repair. Currently all bone fracture repair therapeutic require local administration during surgery. However, the population that need the most assistance in repair bone fractures are not eligible for surgery. So, it was our goal to design an inject-able therapeutic to assist in bone fracture repair to reduce the invasiveness. The injectable nature of it allows for repair administration of the bone anabolic and for therapeutic effect throughout the entire bone fracture healing process. Targeting it to the bone fracture site reduces the toxicity and increases the efficacy. METHODS/STUDY POPULATION: METHODS To achieve the above objective, a bone mineral-(hydroxyapatite-) targeting oligopeptide was conjugated to the non-signaling end of an engineered parathyroid hormone related protein fragment 1-46 with substitutions at Glu22,25, Leu23,28,31, Aib29, Lys26,30 (ePTHrP). The negatively charged oligopeptide has been shown to target raw hydroxyapatite with remarkable specificity, while the attached PTHrP has been demonstrated to induce sustained and accelerated bone growth under control of endogenous morphogenic regulatory factors. The conjugate's specificity arises from the fact that raw hydroxyapatite is only exposed whenever a bone is fractured, surgically cut, grafted, or induced to undergo accelerated remodeling. The hydroxyapatite-targeted conjugate can therefore be administered systemically (i.e. without invasive surgery or localized injection) and still accumulate on the exposed hydroxyapatite at the fracture site where it accelerates the healing process

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