Year-Out Research

Marguerite Maguire

Objectives: Many women who receive a diagnosis of fetal anomaly in the second trimester choose to terminate. Grief over termination for fetal anomaly has been shown to be severe however, little is known about how women define and experience this grief over time.

Study Design: From March 2012 to October 2013, we conducted qualitative phone interviews of 17 women from UCSF and University of Michigan at 1-3 weeks, 3 months and 1 year after second-trimester termination for fetal anomaly. All women chose their method (D&E or induction). We used a generative thematic approach to analyze the transcripts using NVivo software program.

Results: Seventeen participants completed at least one interview. All women reported grief at their initial interview but moved to coping throughout the year. Themes throughout the interviews include self-blame, guilt, social isolation, and grief triggered by reminders of pregnancy. We observed no difference in grieving based on method.

Conclusions: Pregnancy termination in the second trimester for fetal anomaly represents a loss similar to miscarriage or death of a loved one. However, this type of pregnancy loss is unique in that certain aspects of grief are related to participants' active role in the decision to end the pregnancy. Unlike grief after miscarriage, grief after pregnancy termination is associated with real and perceived stigma around terminating a pregnancy. This stigma is associated with feelings of self-blame, guilt and social isolation, which have been shown to compound the grieving process.

Year-Out Research

Tyrrell, Jamie

Preceptor:
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Teaching Theatre and Medicine

Abstract: Doctors, patients, and diseases have been the subject of a number of popular, famous, and infamous plays and television shows. The representations of the practitioners, the medical scientists, the patients, the sickness, the treatments, and the ethical dilemmas in these stories reflect the historical moment and the cultural perceptions (and misperceptions?), expectations, and anxieties about the medical profession. By teaching medical students to appreciate the ability of theatre and television to both reflect and influence public perception, they will be to recognizing the impact of dramatic portrayals of medicine on their patients' expectations of a medical experience.

Objectives: To provide an overview of theatrical representations of doctors and medical experiences and an understanding of the historic context in which the plays were written. To provide medical students with a context for assessing dramatic representations of doctors and medical experiences in contemporary media.

Methods: The "Playing Doctor from Shakespeare to Scrubs" medical humanities seminar exposed second-year medical students to medically-themed theatrical texts from the sixteenth through twenty-first centuries. Students presented dramatic readings from plays such as *All's Well That Ends Well* by William Shakespeare, *The Doctor's Dilemma* by George Bernard Shaw, *Angels in America* by Tony Kushner, and *Wit* by Margaret Edson. Students presented excerpts from television and film portrayals of medicine and facilitated discussions about the historical context and medical themes.

YEAR-OUT RESEARCH

Reiter, Nicholas

Preceptors:
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Toxicity Study of anti-VEGF Treatments for Macular Degeneration

Abstract:

Age-related macular degeneration (AMD) is the leading cause of blindness in developed countries, affecting about 2% of Americans[9]. Current treatment includes intraocular injections of ranibizumab (Lucentis, Genentech), aflibercept (VEGF Trap-Eye, Regeneron), and bevacizumab (Avastin, Genentech). Ranibizumab was the first of the three to be FDA approved and was shown to be safe and superior to previous treatments in 2005 clinical trials[2,10]. Later, aflibercept was found to be of similar effectiveness and safety as ranibizumab in 2012 RCTs[4,16]. Avastin, FDA approved to treat colon cancer, has been used off label for intraocular use since 2005 but does not have similarly large clinical trials as Lucentis and VEGF Trap-Eye to support its safe intraocular use, though a large retrospective study[3] and an RCT[5] showed bevacizumab to be no more harmful than ranibizumab. Some *in vitro* studies have found no differences between the three treatments on cell morphology, viability, or cell death in a variety of cornea and retinal cell lines[1,7,8,13,15,18]. However, for unknown reasons, other studies have demonstrated a cytotoxic effect of bevacizumab on retinal pigment epithelial cells, choroidal endothelial cells, fibroblasts, and trabecular meshwork[6,10] while ranibizumab had no adverse affects on the same cell lines[12,15].

Objectives: To determine *in vitro* cytotoxicity of bevacizumab, ranibizumab, and aflibercept on ARPE-19 cells.

Methods: Cellular toxicity was assessed through cell viability (MTT), proliferation (BrdU), permeability (TER), apoptosis (TUNEL), and intracellular accumulation (Cy3 conjugation).

Results: Bevacizumab inhibited cellular proliferation in BrdU studies, and along with aflibercept accumulated intracellularly 1.5 fold compared to control. No differences were found in MTT, TER, or TUNEL assays between the three treatments.

Conclusions: Bevazicumab may inhibit RPE cell proliferation, possibly related to its intracellular accumulation. Although aflibercept was found to acculumate as well, no adverse affects on RPE cells were observed. Though no direct correlation can be made with clinical safety, this data shows that future work on anti-VEGF toxicity should continue with these relatively new drugs.

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YEAR-OUT RESEARCH

Miller, Katherine

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The Affect of Late Infection and Antibiotic Treatment on Capsular Contracture in Silicone Breast Implants: A Rat Model

Objective
Despite strides being made in current research to combat capsular contracture via disruption of biofilms and reduced contamination at the time of implant,[1,2,3] capsular contracture continues to occur months to years after implantation with no sign of these early complications.[4,5] Up until this point, no research has been carried out to attempt to identify a link between a remote infection established well after implantation, the hematogenous spread of bacteria to a capsule, and capsular contracture, leaving a gap in clinical guidelines for the treatment of breast implant patients. This experiment is the first to assess whether late infections increase the incidence of capsular contracture and if treatment of these infections can reverse this effect in an in vivo rat model.

Methods
Three groups of female Wistar rats (n=42) received two silicone implants in separate dorsal, subcutaneous pockets. All groups except control underwent injection of a human strain of Methicillin-sensitive *Staphylococcus aureus* (MSSA) at least 30 days after implantation, allowing for physiologic capsule formation. The infection group received a peritoneal injection, inducing a transient bacteremia, the treated group received a course of antibiotics following bacterial inoculation, and a final group received no intervention and served as control.

Results
Implants were removed 4 months after insertion with capsules measured for thickness and sent for bacterial quantification. Compared to both the control and treated groups, capsule thickness in the infection group was statistically greater ($p < 0.05$), a difference not observed between treated and control groups. Additionally, a statistically significant positive correlation was found between capsule thickness and bacterial count ($R=0.614$, $p<0.01$).

Conclusions
The difference in thickness between the control capsules and those from the infection group is an indication that bacterial contamination of a capsule from a late infection may increase the incidence of capsular contracture and suggests that treating these late infections could in fact prevent this complication.

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Year-Out Research

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Title: Human Vection Perception Using Inertial Nulling and Certainty Estimation

Abstract: When an object is moved in visual space there are two possible perceptions: 1) the viewer perceives external object motion or 2) the viewer perceives self-motion (vection). The latter occurs if the object motion involves a significant portion of the visual field. Individuals with visual motion sensitivity disorders such as migraine may be especially susceptible to vection. We aimed to expand the current understanding of vection by examining the effect of visual field movement (VFM) duration on the perception of subsequent self-motion. We hypothesized that longer duration VFM would produce greater vection and would thus require greater vestibular stimulation to null the perception of self-motion. To test this, we examined how VFM influenced threshold and bias. We also collected subject-reported estimations of vection, and hypothesized that longer duration VFM would be perceived as stronger. The relationship of migraine and vection was examined. We recruited 12 healthy adult subjects and examined for history of migraine. Subjects sat on a motion platform. A visual star-field stimulus was presented for varying durations and fore-aft platform motion occurred in the final 1 s of the visual stimulus. Subjects reported the perceived direction of platform motion using a pushbutton device. The magnitude of platform motion was varied across trials in a staircase manner to determine the point of subjective equality (PSE). We calculated the peak velocity of the platform motion stimulus at the PSE as a measurement of bias, and examined relationship of PSE and VFM duration. In a separate trial using identical visual stimuli but no platform motion stimulus, subjects reported certainty and direction of perceived self-motion. The relationship of certainty estimation (CE) and VFM duration was examined. Increased VFM duration significantly increased PSE ($p = .007$) and CE ($p < .0001$). The net effect of direction was not significant in either condition. Diagnosis of migraine significantly increased perception of self-motion by CE ($p = .01$) but not PSE. These results suggest that vection is increased by longer duration visual stimuli, and that history of migraine plays a significant role in self-motion perception.
Objectives: This project aims to expand our current understanding of vection by quantifying it using actual motion and comparing this value to subjects' subjective estimations of vection strength. Individuals with motion sensitivity disorders and other vestibular disorders, such as migraine, may be especially susceptible to migraine. If this is the case, the accurate measurement of vection may serve as part of a diagnostic test for vestibular disorders.
Methods: Twelve healthy individuals (7M, 5F) aged 19 to 67 (mean 39.25 ±18.32) were recruited. In Part One of the experiment, motion stimuli were delivered in complete darkness using a 6-degree of freedom Hexapod Motion Platform (HMP) coupled to the visual display. Subjects were secured in place with the head anchored. A visual stimulus consistent with moving through a star field was presented at a constant velocity of ±20 cm/s for 0 (no visual stimulus), 1, 2, 4, or 8 seconds. Platform motion in the forwards or backwards direction occurred in the final 1s of the visual stimulus. Subjects reported perceived direction using a pushbutton device. The magnitude of platform motion was varied in a staircase manner. Peak platform velocity at the PSE was determined. In Part Two of the experiment, identical visual stimuli to those previously described were delivered with no motion stimulus. Subjects reported the perceived direction and magnitude of self-motion on a scale of 0 (none) to 100 (very compelling).

Results: Increased visual stimulus duration significantly increased vection by our two methods of measurement, PSE (p = .007) and CE (p < .0001). The diagnosis of migraine was significantly increased by measurement of vection by CE (p = .01) but not PSE.
Conclusions: These results suggest that vection is increased by longer duration visual stimuli, and that history of migraine plays a significant role in self-motion perception.