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Attitudes toward fertility and fertility preservation in women diagnosed with glioma

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ATTITUDES TOWARD FERTILITY AND FERTILITY PRESERVATION IN
WOMEN DIAGNOSED WITH GLIOMA

by

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ATTITUDES TOWARD FERTILITY AND FERTILITY PRESERVATION IN WOMEN DIAGNOSED WITH GLIOMA

RACHEL STINER

ABSTRACT

**Background:** Gliomas are the most common primary brain malignancy, with more than 16,000 patients diagnosed every year (Ostrom, et al., 2015). Outcomes vary widely depending on tumor grade and treatment, and have been steadily improving with the advent of new therapeutics. Glioma patients frequently undergo chemotherapy to remove residual tumor after surgery, and many of these cytotoxic therapies are known to affect rapidly dividing cells such as ovarian follicles (Vassilakopoulou et al., 2016). The negative effects of chemotherapy on fertility have been demonstrated in patients with breast and colorectal cancer (Bines, et al., 1996; Avastin Prescribing Information). Additionally, infertility has been linked with decreased quality of life, primarily in women (O'Moore et al., 1983; Greil, 1997). Fertility treatments are available for women undergoing cancer treatment, however it is unknown whether these treatments are routinely discussed with glioma patients before initiating chemotherapy.

**Objective:** The primary goal of this study was to assess whether female glioma patients are being effectively counselled on their possible loss of fertility and their choices for fertility treatment prior to beginning chemotherapy. To this end, it was also important to understand the barriers preventing patients from obtaining
information related to their fertility. Another principle goal of this study was to describe the effects of chemotherapy on a sample of women with glioma. Finally, this study sought to understand the priorities of women with glioma in regards to family planning, and to address these priorities in the context of a comprehensive fertility preservation discussion.

**Methods:** To assess these endpoints, a survey was designed and delivered to patients being treated at the Neuro-oncology clinic of the University of California, San Francisco. Eligible candidates were identified prior to a clinic visit, and patients were asked whether they would like to participate in the survey. Consenting patients then completed the survey at home or in the clinic. Seventy two women completed the survey. Data was analyzed using STATA Software Version 10.0.

**Results:** Analysis of the survey results showed that only 35% of women receiving chemotherapy reported having a discussion regarding fertility preservation prior to beginning treatment. Of those who reported having this discussion, only 80% were aware that chemotherapy could negatively affect their fertility. Many women reported that while fertility preservation was not important to them at the time of diagnosis, it was a priority for them at the time of survey completion. Most women surveyed expressed a desire to have a fertility preservation discussion with a reproductive specialist.

**Conclusions:** The data obtained in this study suggest a lack of understanding of the negative effects of chemotherapy which may be addressed with a more comprehensive fertility discussion with glioma patients prior to beginning
treatment. Although interest in having children tends to decrease after cancer treatment, the majority of respondents still report wanting a child after treatment. The priorities of women in the study reflect a concern for the health of their future offspring which may be best addressed prior to beginning treatment in order to increase their chances of conceiving at a later date.
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LIST OF ABBREVIATIONS

CCNU .......................................................................................................................... Lomustine
GBM ............................................................................................................................. Glioblastoma
IVF ............................................................................................................................... In Vitro Fertilization
POF ............................................................................................................................... Premature Ovarian Failure
TMZ .............................................................................................................................. Temozolomide
UCSF ............................................................................................................................ University of California, San Francisco
WHO .............................................................................................................................. World Health Organization
INTRODUCTION

*Gliomas are the most prevalent primary brain malignancy*

Gliomas are tumors arising from the glial, supportive cells of the brain. The vast majority (80%) of all primary brain malignancies are gliomas. Classification of these tumors is most commonly done by the World Health Organization (WHO) grading system, which grades tumors from Grade I (best prognosis) to Grade IV (worst prognosis) based on tumor histology (“Tumor Grading and Staging”). Grade I and II tumors are considered to be “Low Grade Gliomas”, and Grade III and IV tumors are considered to be “High Grade Gliomas”. Using the WHO grading system, several features are taken into account to determine a tumor’s grade: atypical cells, mitoses, endothelial proliferation, infiltration and necrosis. If a tumor contains none of these characteristics, it is classified as a Grade I (benign) glioma. Grade I gliomas do not have infiltrative features and are the only type of glioma that may be “cured” by surgery alone. Tumors that contain one of these characteristics are classified as Grade II and they are considered malignant. Finally, tumors that contain two or more of the above characteristics are classified as Grade III or IV and considered high grade (Grier, 2006).

In adults, gliomas may be subdivided into astrocytomas, oligodendrogliaomas, or mixed oligoastrocytomas depending on the cell type of origin. Ependymomas are a fourth type of glioma that are relatively rare, making up only 2-3% of primary brain tumors (“Ependymoma”).
Grade II gliomas usually display hypercellularity, but do not contain areas of necrosis. These tumors make up approximately 15% of all primary gliomas, and tend to afflict patients aged 20-50, carrying a median survival rate of 5-7 years (Pouratian & Schiff, 2010; Aijian & Recht, 2014).

Grade III gliomas, in addition to displaying hypercellularity, are more pleomorphic in character, and cells of these tumors exhibit a wide range of variability in the size and shape. The mean age of onset for grade III gliomas is 45 years, and median survival time for patients with anaplastic astrocytoma is 3-4 years (Pan & Prados, 2003; Stupp et al., 2005).

Grade IV gliomas, also called glioblastomas (GBM) are the most common, accounting for 55% of primary brain tumors. These tumors have a higher labelling index than grade III tumors, corresponding to a faster rate of cell division and more aggressive growth (Pan & Prados, 2003). The mean age of onset of GBM is 54 years (Pan & Prados, 2003). Median survival time for individuals with GBM is approximately 14.6 months if the patient receives standard radiation and chemotherapy (Stupp et al., 2005).

Although tumor grade is an important prognostic factor, other factors that are essential to consider are age at onset, tumor location, extent of resection, and treatment (Edge & AJCC, 2010). In addition, presence or absence of molecular markers is an important component of understanding a patient’s tumor. The presence of a certain molecular marker may make a patient more likely to respond
to a particular therapy. For this reason, molecular studies are often performed immediately after resection, and may contribute to prognosis.

**Standard treatment for glioma includes surgery, radiation, and chemotherapy**

Regardless of tumor grade and histopathology, the first course of treatment is almost always maximal safe surgical resection of the tumor. Exceptions are made in some low grade cases when resection may not confer a clear benefit, or when a tumor is deep-seated or in an eloquent area that increases risk of postoperative neurological deficits (Raizer & Parsa, 2015). It has long been shown that extent of resection correlates with increased overall survival, increased progression-free survival and, in the case of low grade gliomas, increased time to malignant transformation. However, the infiltrative nature of gliomas prevents a true “complete removal” of the tumor through surgery alone (McGirt et al., 2009).

Surgical removal not only reduces mass effect (pressure and swelling, causing symptoms) but enables a pathological examination of the tumor tissue, which helps inform clinical decision-making.

Radiation is considered the best treatment method following surgery. Although it carries its own risks of toxicity, radiation confers an advantage over systemic chemotherapy that side effects other than fatigue are localized to the tissue being irradiated (Lutz et al., 2007) Once the gross tumor volume is determined, a clinical target volume which includes areas of subclinical infiltrative disease is defined. Radiation oncologists will then determine a planning target volume which
allows for a margin of error (Burnet, 2004). Patients are usually treated with multiple “fractions” of radiation, which has been shown to be more effective than one large single dose or a few large doses (Lutz et al., 2007). The goal of radiotherapy is to target as much of the tumor as possible without affecting the surrounding healthy tissue. However, some healthy tissue is unavoidably affected and side effects of this stray radiation include necrosis, edema, cognitive decline, motor deficits, and personality changes (Veninga et al., 2001). Edema can often be managed with the use of corticosteroids (Veninga et al., 2001). Because glioma radiation treatment is localized to the affected brain area, side effects associated with whole body radiation, such as damage to early responding tissues like the ovaries and uterine lining, are not observed.

In many cases, radiation may be given concurrently with chemotherapy. The current standard of care for GBM is 6,000 cGy of radiation given over 30 days along with concurrent temozolomide (TMZ) and six months of adjuvant temozolomide (Raizer & Parsa, 2015). Temozolomide is an alkylating agent that attaches a methyl group to the purine bases of DNA. Because TMZ is a systemic therapy that targets rapidly dividing cells, it commonly causes gastrointestinal toxicity due to the highly proliferative nature of the gastrointestinal lining. This type of therapy also causes damage to bone marrow leading to low white blood cell counts. In a study of 300 glioma patients, nausea, vomiting, and anorexia were shown to be the most common side effects of TMZ (Bae et al., 2014). There is also evidence that TMZ may cause damage to ovarian follicles (see below).
Another common therapy used in treatment of both low and high grade gliomas is the combination of procarbazine, lomustine (CCNU), and vincristine - shortened to “PCV”. Both procarbazine and CCNU are alkylating agents similar to TMZ. Vincristine is a vinca alkaloid which works by preventing chromosome separation during mitosis, leading to cell death. Like alkylating agents, vincristine targets rapidly dividing cells and causes many of the same side effects.

Bevacizumab is a monoclonal antibody which blocks growth of new blood vessels to tumor tissue. It is commonly used to treat recurrent glioblastoma, either as a monotherapy or in combination with another chemotherapeutic agent. Common side effects associated with bevacizumab are proteinuria and hypertension (Gilbert et al., 2014). Bevacizumab is used to treat other types of cancer besides glioma, notably kidney and colon cancer. Recently a study of patients with colorectal cancer suggested that bevacizumab may cause premature ovarian failure in female patients, and this warning has been added to the prescribing information for the drug (Avastin Prescribing Information).

**Some cancer treatments affect patients’ ability to reproduce**

The ability to conceive is dependent on the health of the ovaries, uterus, hypothalamic-pituitary axis, and overall health of the body. Cancer itself, radiation therapy, and cytotoxic treatments can impair the health of any of these systems. Some studies report that up to half of women experience menstrual cessation with cancer treatment (Goodwin et al., 1999). Amenorrhea is the complete loss of
menses, while oligomenorrhea is defined as light or infrequent menstrual periods. While normal menses do resume in some women after treatment, others continue to experience amenorrhea or oligomenorrhea. Even the resumption of normal menses does not guarantee fertility, as up to 40% of women who resumed their menstrual cycle after cytotoxic treatment were found to be infertile (Vassilakopoulou et al., 2016).

Premature ovarian failure (POF) is the loss of ovarian function before the age of 40, due either to a lack of ovarian follicles or a failure of primordial follicles to mature (Daan et al., 2015). The ovaries of women with POF show cortical fibrosis, deformation of capillaries supplying follicles, and in some cases defects in mature follicles. Cytotoxic drugs can cause POF by impeding cell division or by causing direct damage to mature follicles (Vassilakopoulou et al., 2016). While other rapidly-dividing areas may recover after cessation of cytotoxic treatments, the ovaries are unable to do so (Falcone et al., 2004).

Many chemotherapeutic agents have been implicated in causing POF. In a study of patients with colorectal cancer, 34% of female patients being treated with bevacizumab showed ovarian failure during treatment versus only 2% of female patients on the same regimen without bevacizumab. After cessation of treatment, 22% of female patients treated with bevacizumab recovered ovarian function as determined by resumption of a menstrual cycle, a positive pregnancy test, or demonstration of low FSH serum level (Avastin Prescribing Information). However,
these indicators alone do not give information on the health of the ovarian follicles or the number of follicles remaining.

Alkylating agents including temozolomide and CCNU have also been linked to POF. Taking into account the mechanism of action of these drugs, which is to alkylate newly copied DNA, it is unsurprising that they affect rapidly-dividing cells such as ovarian follicles. A study of patients who underwent treatment for childhood cancer found that those treated with CCNU or other alkylating agents were significantly less likely to have been pregnant than patients who were not treated with alkylating agents (Green et al., 2009). However, at least one study has shown that the gonadotoxic profile of TMZ is less severe than that of other alkylating agents such as cyclophosphamide or busulfan (Sitruk et al., 2010).

Patient age is also directly linked with increased risk of POF, with one study showing that among patients receiving chemotherapy, those greater than 40 years old had significantly higher rates of amenorrhea than those age 40 and younger (Bines, Oleske & Cobleigh, 1996). Since the number of remaining ovarian follicles declines steeply with age, older women are at a higher risk for permanent ovarian failure.

**Infertility is associated with decreased quality of life**

Infertility is commonly defined as the inability to conceive after trying to do so for one year. Several studies have sought to examine the effects of infertility on quality of life, although the results of these studies considered together are
somewhat equivocal. Some studies have shown that infertile patients are more likely than their fertile peers to experience psychological distress, sensitivity, and depression (O’Moore et al., 1983). While other studies evaluating personality disorders in these patients have showed ambiguous results, it is generally accepted that infertile patients do experience increased distress in comparison to fertile controls. It is also well known that infertility causes more stress in female patients than it does in male patients (Greil, 1997).

**Fertility preservation methods are available**

Options do exist for women who would like to take steps to preserve their fertility prior to undergoing radiation or chemotherapy. In vitro fertilization (IVF) involves stimulating the ovaries, collecting the mature oocytes, and immediately fertilizing them in vitro before freezing. This method, while one of the most established and successful, has the downside of requiring sperm immediately after harvesting the oocytes. Therefore, it is not always a viable option for single women who wish to conceive later in life. In vitro fertilization also requires 10-14 days for follicular development, which may not be possible for patients needing to undergo chemotherapy immediately (Levine, Canada & Stern, 2010; Vassilakopoulou et al., 2016).

Another option that is more amenable to single women is mature oocyte cryopreservation. Using this method, the ovaries are stimulated to produce mature follicles, which are then harvested and frozen. While success rates of mature oocyte
cryopreservation are lower than embryo cryopreservation, this method is becoming more successful and up to 60% of oocytes can be expected to survive the thawing process at a later date. Of those oocytes that successfully thaw, roughly 33% to 50% will be successfully fertilized and implanted (Chen, 1986).

For women who require immediate chemotherapy following diagnosis, there are two options currently available, although both are less studied and established than traditional IVF methods. One option is harvesting immature oocytes rather than mature oocytes and freezing until fertilization is desired. While this procedure may be done immediately (without the 10-14 day delay), it also carries a lower success rate than mature oocyte preservation (Suikkari, 2008).

Finally, an emerging method of fertility preservation is ovarian tissue freezing and grafting. Using this method, either an entire ovary or part of an ovary is removed laparoscopically and frozen after being sliced thinly. After the patient has undergone treatment for their cancer and has recovered to an acceptable state, the tissue is grafted onto the existing ovary or the uterine wall. This method ensures the availability of numerous follicles and can also be performed without the 10-14 delay in treatment (Gook et al., 2005; Oktay et al., 1997).
SPECIFIC AIMS

It is estimated that in 2015 alone, there were over 16,000 new cases of primary glioma in the United States (Ostrom, et al., 2015). Although it is widely accepted that cancer chemotherapy causes gonadotoxicity, these effects have not been studied in glioma patients. In addition, it is unknown whether female glioma patients are receiving adequate counseling regarding their options for fertility preservation, or whether they are even aware that treatment may affect their fertility. Some studies have shown that infertility negatively impacts quality of life, but the specific priorities and values of glioma patients and how they change due to cancer diagnosis or fertility status have not been investigated (Schover et al., 1999).

This paper seeks to achieve the following aims:

1. Describe how chemotherapy affects fertility of women with gliomas.
2. Examine whether female glioma patients are being adequately counseled on the possible side effects of chemotherapy on their fertility and their options for fertility treatment.
   1. Understand the barriers to communication that may be causing inadequate fertility counseling prior to cancer treatment.
3. Describe the priorities of women diagnosed with glioma regarding family planning and future childbearing.
METHODS

Study Population and Eligibility

In order to assess the fertility outcomes, priorities, and effectiveness of fertility counseling in women with glioma, we used data collected from the “Fertility in Women with Primary Brain Malignancies” study conducted at the University of California, San Francisco (UCSF). This study was approved by the UCSF Institutional Review Board and was designed to analyze fertility in women with glioma, as well as understand whether these patients were receiving adequate counseling regarding fertility treatment prior to undergoing treatment for their cancer.

Eligible patients were women between the age of 18-45 at time of diagnosis who had a primary brain malignancy that was WHO grade II, III, or IV. Potentially eligible women were identified at check-in prior to their visit at the UCSF Neuro-oncology clinic. These patients were then given a description of the study and, if interested, were consented in clinic by a trained researcher. Consented patients were then given the link to the online study, which they could choose to complete either after their clinic visit at a provided computer terminal or at home at their leisure. Patients were also given the option to complete the survey on an iPad provided to them in the clinic, or to complete the survey in paper format at home or at the clinic. If participants had not completed the survey prior to returning to the clinic for a second visit, they were reminded to do so. A final reminder was given at the third visit if the participant had failed to complete the survey. Surveys were completed between October 27, 2010 and December 5, 2013. This survey was cross-
sectional in nature; women completed the survey at different time points after their diagnosis and during their treatment.

Of 99 women consented to the study, 73 completed the study either in paper or digital format. Of these, one patient gave responses only to the initial demographic information, and did not provide responses to any of the questions in the body of the survey. This patient’s data was not included in the analysis.

**Effect of Chemotherapy on Fertility**

One of the primary aims of the survey was to analyze the effect of chemotherapy on patient fertility. This was done using a targeted set of questions that investigated whether patients had tried to have a child after completing cancer treatment and if they had successfully conceived. Patients were also asked whether fertility treatment was used and if so, which methods were utilized. Additionally, patients were asked to report changes in their menstrual cycles that occurred since cancer treatment began. Unfortunately, there were complications with questions designed to assess the effect of chemotherapy on fertility leading to a lack of data in this area. Few women reported attempting to conceive after treatment and among these women there was low response toward questions assessing their fertility. One notable exception is the assessment of menstrual changes since treatment initiation, and the results of this data will be discussed.
**Determination of Prevalence and Effectiveness of Fertility Counseling**

Several survey questions were designed to understand the circumstances surrounding pre-treatment fertility preservation discussions. Patients were asked whether they had a discussion regarding fertility preservation prior to treatment, and if so, who initiated the discussion. Patients also answered questions regarding which parties participated in the discussion, and with whom they would have felt most comfortable discussing the topic. Lastly, patients reported whether or not they were aware that chemotherapy could affect their fertility.

**Priorities of Women with Glioma**

One of the goals of the project was to understand the priorities of women with glioma in relation to family planning and childbearing and how these priorities were influenced by their diagnosis. We asked women to rank the following categories in order of importance both before their diagnosis and after their treatment: having a child, spending time with loved ones, career, hobbies, health, and service. Women were asked to give a priority of 1 (most important) to 6 (least important), and they were also allowed to give a “tie” to two or more categories. Since patients only completed the survey once, and only after their treatment was initiated, they were asked to recall their priorities prior to diagnosis to the best of their abilities.

In order to more precisely understand the desires and concerns of women regarding family planning and childbearing, we asked participants to rank a series
of statements based on how desirable they were. Women gave a rank of 0 (not
desirable) to 10 (most desirable thing imaginable) for 18 statements relating to
being pregnant and having a child.

Similarly, women were asked to rank the undesirability of 17 statements
relating to aspects of pregnancy and motherhood. Participants ranked statements
from 0 (desirable) to 10 (most undesirable thing imaginable). Rankings for both
categories (desirable and undesirable) were independent of one another and the
same score could be assigned to multiple statements.

Finally, women were asked to indicate how strongly they agreed or disagreed
with six statements regarding feelings toward having a first child or an additional
child. Rankings were given on a scale of 0 (strongly disagree) to 10 (strongly agree).

Statistical Analysis

Survey results were analyzed using STATA Software Version 10.0.
Descriptive statistics including age at diagnosis, tumor grade, and parity were
generated. A chi-square test was performed to test the hypothesis that interest in
having more children did not change before diagnosis to after treatment, regardless
of the patient’s tumor grade.

Data regarding fertility discussions was tabulated and described. A chi-
square test was performed to test the correlation between tumor grade and
awareness that treatment affected fertility.
Priorities before diagnosis and after treatment were analyzed and described. Average scores for each category were calculated, and the difference between the averages was determined. A t-test was performed for each category to test the hypothesis that there was no difference in the average. Average ranking of desirability or undesirability for each category was calculated and data was ordered. Data was evaluated qualitatively to understand general desires and concerns of women regarding childbearing.
RESULTS

Description of the Variables in the Study Population

Demographics

Seventy two women between the ages of 19 and 45 completed the survey between 2010 and 2013. The average age of women completing the survey was 35.3 years old, and the median age was 36 years. Among the study population, 78% identified as White, 7% identified as Hispanic, 6% identified as Asian, 1% identified as African American, and 8% identified as either “more than one race” or “other”. One person declined to state their race. The majority of women taking the survey were in some type of relationship, either married (48%), living with their partner but not married (14%) or significantly involved but not living with their partner (9%). The remainder of the women reported that they were either single (25%) or separated (4%).

Tumor Grade and treatment

Grade 2 gliomas were the most prevalent, representing 49% of those surveyed. Grade 3 gliomas were the second most common, accounting for 33% followed by grade 4 gliomas (GBM) representing 15% of the sample. Two participants noted a grade of “other”. It is possible that women reporting a grade of “other” were those who had experienced a progression of their tumor grade (i.e. their tumor had progressed from grade 3 to 4 during treatment). It is also possible that these women had grade I tumors, although the survey was designed to exclude
women with grade I tumors after this step. In analyses that consider tumor grade, participants reporting a grade of “other” were not considered. The vast majority (89%) of subjects reported receiving surgery for their tumor, while 75% received chemotherapy, 57% received radiation, 13% received all of the treatments listed plus others. One person declined treatment for their tumor.

*Childbearing and Fertility*

Participants were asked to report the number of children that they had at the time of taking the survey. The majority of the participants (57%) were nulliparous (never having given birth), while 18% had one child, 17% had two children, and 8% had three, four, or five children. Participants were asked if they were infertile before they were diagnosed with cancer, however only 21 subjects responded to this question. Five participants (24%) responded that they were infertile, 13 participants (62%) responded that they were not infertile, and 3 participants (14%) reported that they had never tried to conceive. Descriptive statistics are given in Table 1.
Table 1. Descriptive Statistics of the Study Population. The mean and standard deviation are defined for the continuous variables. The frequency (n) and percent are defined for categorical variables.

<table>
<thead>
<tr>
<th>Characteristic (n=72)</th>
<th>Mean (SD) or n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>35.3 (7.06)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>White, Non-Hispanic</td>
<td>56 (78%)</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>5 (7%)</td>
</tr>
<tr>
<td>African-American/Black</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Asian</td>
<td>4 (6%)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (8%)</td>
</tr>
<tr>
<td>Relationship Status</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>18 (25%)</td>
</tr>
<tr>
<td>Significantly Involved but Not Living with Partner</td>
<td>6 (9%)</td>
</tr>
<tr>
<td>Living with Partner but Not Married</td>
<td>10 (14%)</td>
</tr>
<tr>
<td>Married</td>
<td>34 (48%)</td>
</tr>
<tr>
<td>Separated</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Tumor Grade</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>35 (49%)</td>
</tr>
<tr>
<td>3</td>
<td>24 (33%)</td>
</tr>
<tr>
<td>4</td>
<td>11 (15%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>41 (57%)</td>
</tr>
<tr>
<td>Primiparous</td>
<td>13 (18%)</td>
</tr>
<tr>
<td>Multiparous</td>
<td>18 (25%)</td>
</tr>
<tr>
<td>Number of children</td>
<td>0.82 (1.17)</td>
</tr>
<tr>
<td>Cancer treatments received (multiple responses allowed)</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>64 (89%)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>54 (75%)</td>
</tr>
<tr>
<td>Radiation</td>
<td>41 (57%)</td>
</tr>
<tr>
<td>All of the above plus others</td>
<td>9 (13%)</td>
</tr>
<tr>
<td>No treatment</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>
Effect of Cancer Treatments on Fertility

Self-reported infertility

Women were asked questions regarding their fertility before diagnosis and after treatment in order to understand changes that may have occurred due to chemotherapy. Of the 21 women who responded, 5 (23%) reported that they were infertile prior to diagnosis, 13 (62%) reported they were not infertile, and 3 (14%) reported they had not attempted to conceive prior to diagnosis. In addition, four women reported that they received fertility treatment prior to diagnosis, with all four receiving hormonal treatments, and two receiving intrauterine sperm injections.

Only four women reported trying to conceive after completing treatment. Of these women, one was unable to conceive while three did successfully conceive. The unsuccessful patient reported trying to conceive for 10-12 months and did not report using any method of fertility treatment for assistance.

Menstrual changes

In order to understand the frequency of menstrual changes after treatment, participants were asked questions about their menstrual cycle before and after undergoing treatment for their cancer. Of the women who responded, only 6% of women reported having irregular menstrual cycles prior to treatment, while 91% reported regularity and the remaining 3% did not remember. Participants were then asked to describe how their menstrual cycle had changed since undergoing therapy. Subjects chose one answer that best matched their experience out of
thirteen options which included increases and decreases in frequency, changes in amount of bleeding, and changes in menstrual patterns. Of the 59 women who provided a response and who had begun treatment, 56% reported some type of menstrual change since initiating cancer treatment, while 36% reported no change. The remaining 8% reported that they either did not know or their response did not fit into one of the categories defined. Of those patients who had chemotherapy, 69% reported some type of change to their menstrual cycle, while only 22% of women who did not have chemotherapy (but who may have had surgery and/or radiation) reported a change. A chi-square analysis showed that this was significant with p=0.009, indicating a correlation between being treated with chemotherapy and experiencing menstrual changes.

*Determination of Prevalence and Effectiveness of Fertility Counseling*

A central goal of the study was to assess whether fertility counseling was made available to patients prior to their initiation of any cancer treatments, and to identify any obstacles preventing this discussion. Participants were asked whether they discussed fertility preservation prior to beginning treatment, and only 30% reported that they had. Approximately 61% reported not having a fertility preservation discussion, and 9% did not remember whether they had discussed it. However, of those who received chemotherapy, 35% stated that they had a fertility preservation discussion, while only 17% of patients that did not receive chemotherapy reported having this discussion. This result was not statistically
significant with $p=0.10$. This may reflect the small sample size, or may indicate that those undergoing chemotherapy were not in fact more likely to discuss fertility preservation. In this sample, patients with grade 2 gliomas were statistically less likely to have had a fertility preservation discussion than patients with grade 3 or 4 gliomas ($p=0.015$), however these patients were also statistically less likely to have undergone chemotherapy ($p=0.004$).

Patients were also asked whether they knew that cancer treatments could affect their fertility, and 63% reported awareness of this fact. Of those patients who had a fertility discussion, 80% were aware of the risks to their fertility. However, among patients who did not have a fertility discussion, only 55% were aware of the risks posed by chemotherapy. A chi-square analysis was performed to analyze whether patients were more likely to be aware that treatments affected their fertility if they had a fertility preservation discussion and this result approached significance at $p=0.054$. In order to determine whether patients were more likely to be aware of treatment effects on their fertility if they had a higher grade tumor, a chi-square test was performed and the results were statistically significant with $p=0.01$. While only 47% of participants with grade 2 tumors were aware, 77% of those with grade 3 tumors were aware, and 90% of those with grade 4 tumors reported awareness. This result was still significant after controlling for whether individuals had undergone chemotherapy ($p=0.02$).

Several follow-up questions were asked of the 21 patients who reported having this discussion in an attempt to better understand the counselling that did
occur. Patients were asked who brought up the issue of fertility preservation, and 52% reported that their doctor brought it up, 33% reported that their family member brought up the issue, and 52% reported that they themselves raised the discussion (options were not mutually exclusive). This subset of patients was further asked to report with whom they had this fertility preservation discussion, and again options were not mutually exclusive. Patients were most likely to engage in the conversation with their oncologist, followed by their gynecologist, reproductive specialist, nurse, and social worker (Table 2). One patient reported having the discussion, but not remembering with whom it occurred, and another patient reported that they had the discussion with another health professional not listed. Most patients who had this discussion reported that they would have felt most comfortable having the discussion with a reproductive specialist (62%), however a sizable group reported that they would have preferred discussing fertility preservation with their oncologist (38%).

To better understand the barriers women faced in having a discussion regarding their fertility, participants were asked why they did not initiate a discussion with their doctor and thirty eight women provided responses. Fourteen women (37%) reported that fertility preservation was not important to them, even at the time of taking the survey, while 21 (55%) women reported that fertility preservation was not important to them initially but was important at the time of the survey. One (3%) woman reported that she was embarrassed to initiate the
discussion with her doctor, while three (8%) women were concerned with taking up their doctor’s time for this discussion.

**Table 2. Details of the Fertility Discussion.** Responses to fertility discussion questions are tabulated below. The number of participants responding to each question is listed in the right column.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD) or n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to treatments, was fertility preservation discussed?</td>
<td>N=69</td>
</tr>
<tr>
<td>Yes</td>
<td>21 (30%)</td>
</tr>
<tr>
<td>No</td>
<td>42 (61%)</td>
</tr>
<tr>
<td>I Don’t Know/I Don’t Remember</td>
<td>6 (9%)</td>
</tr>
<tr>
<td>If yes, who brought up the discussion?</td>
<td>N=21</td>
</tr>
<tr>
<td>Doctor</td>
<td>11</td>
</tr>
<tr>
<td>Family Member</td>
<td>7</td>
</tr>
<tr>
<td>Patient</td>
<td>11</td>
</tr>
<tr>
<td>If yes, with whom did you have the discussion?</td>
<td>N=21</td>
</tr>
<tr>
<td>Oncologist</td>
<td>17</td>
</tr>
<tr>
<td>Gynecologist</td>
<td>7</td>
</tr>
<tr>
<td>Reproductive Specialist</td>
<td>6</td>
</tr>
<tr>
<td>Nurse</td>
<td>2</td>
</tr>
<tr>
<td>Don’t Remember</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
</tr>
<tr>
<td>With whom would you have felt most comfortable having the discussion?</td>
<td>N=21</td>
</tr>
<tr>
<td>Oncologist</td>
<td>8 (38%)</td>
</tr>
<tr>
<td>Reproductive Specialist</td>
<td>13 (62%)</td>
</tr>
</tbody>
</table>
Priorities of Women with Glioma Regarding Childbearing and Family Planning

Another major goal of the study was to evaluate the priorities of women diagnosed with glioma, and to understand how these priorities affected their decisions regarding fertility preservation and childbearing. Women were asked whether they were interested in having more children both before diagnosis and after treatment. Women were more likely to report wanting more children before their diagnosis (54%), versus after their diagnosis (35%). Women were more likely to report that they were not interested in having children after their treatment, with 28% responding negatively versus only 16% responding negatively prior to diagnosis. However, they were also more likely to report that they were “considering” having more children, with 33% responding in this manner versus only 21% of subjects giving this response prior to diagnosis. A comparison of the answers given before diagnosis and after treatment is given in Table 3. The subset of patients who gave responses both before diagnosis and after treatment and answered either “yes” or “no” were evaluated separately and a chi-square test revealed a significant difference in proportion of response (Table 4).

Table 3. Interest in Having More Children. Responses to the question “Are you interested in having more children?” either before diagnosis or after treatment are tabulated below. The sample size for each question is listed in each column.

<table>
<thead>
<tr>
<th>Response</th>
<th>Before Diagnosis (n=71)</th>
<th>After Treatment (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>38 (53.5%)</td>
<td>14 (35%)</td>
</tr>
<tr>
<td>No</td>
<td>11 (15.5%)</td>
<td>11 (27.5%)</td>
</tr>
<tr>
<td>Considering</td>
<td>15 (21.1%)</td>
<td>13 (32.5%)</td>
</tr>
<tr>
<td>Hadn’t thought about it</td>
<td>7 (9.9%)</td>
<td>2 (5.0%)</td>
</tr>
</tbody>
</table>
Table 4. Interest in Having More Children, Subset. Responses to the question “Are you interested in having more children?” either before diagnosis or after treatment are tabulated below for those who answered either “yes” or “no” at both time points.

<table>
<thead>
<tr>
<th>Response</th>
<th>Before Diagnosis (n=34)</th>
<th>After Treatment (n=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>29 (85%)</td>
<td>23 (68%)</td>
</tr>
<tr>
<td>No</td>
<td>5 (15%)</td>
<td>11 (32%)</td>
</tr>
</tbody>
</table>

Participants were also asked to rank six categories in order of importance before diagnosis and after treatment, with 1 representing the most important item and 6 representing the least important item. On average, women reported that “Spending time with loved ones” was their top priority both prior to diagnosis and after receiving treatment. On average, this category became even more important after treatment, however this change was not statistically significant. T-tests were conducted to evaluate the change in average ranking for each category prior to diagnosis and after treatment, and four changes were significant with p<0.05. “Having a child” and “Career” both became less important with average changes of 0.51 points and 0.81 points, respectively. Both “Health” and “Service” became more important, with average changes of 0.84 and 0.31 respectively. On average, “Hobbies” became slightly more important after treatment, however this change was not statistically significant. Average changes in importance and the p-values for these t-tests are given in Table 5.
Table 5. Average Ranking of Priorities. Category rankings on a 1-6 scale were averaged over the study population. The difference between each average ranking before diagnosis and after treatment was tabulated and a t-test was performed to test whether this difference was significant. Each average is listed along with the difference between averages and the associated p-value. Significant p-values are bolded.

<table>
<thead>
<tr>
<th>Response</th>
<th>Before Diagnosis</th>
<th>After Treatment</th>
<th>Average Difference (SD)</th>
<th>P value of T-Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Having a Child</td>
<td>3.7 (1.9)</td>
<td>4.3 (1.8)</td>
<td>-0.51 (2.0)</td>
<td><strong>0.024</strong></td>
</tr>
<tr>
<td>Spending Time with Loved Ones</td>
<td>2.2 (1.4)</td>
<td>2.0 (1.2)</td>
<td>0.23 (1.2)</td>
<td>0.103</td>
</tr>
<tr>
<td>Hobbies</td>
<td>4.2 (1.1)</td>
<td>4.2 (1.1)</td>
<td>0.05 (1.2)</td>
<td>0.7419</td>
</tr>
<tr>
<td>Career</td>
<td>3.0 (1.6)</td>
<td>3.8 (1.4)</td>
<td>-0.81 (1.8)</td>
<td><strong>0.0003</strong></td>
</tr>
<tr>
<td>Health</td>
<td>2.8 (1.4)</td>
<td>2.0 (1.3)</td>
<td>0.84 (1.5)</td>
<td><strong>0.0001</strong></td>
</tr>
<tr>
<td>Service</td>
<td>4.8 (1.4)</td>
<td>4.4 (1.2)</td>
<td>0.31 (1.2)</td>
<td><strong>0.0265</strong></td>
</tr>
</tbody>
</table>

Participants were asked to give ratings of desirability from 0 to 10 for eighteen categories centering around having a child. Zero represented an undesirable outcome, while ten represented the most desirable outcome imaginable, and these rankings were not mutually exclusive (i.e. a participant could rank every category as “10” if they desired). Of the eighteen categories, the most highly rated was “having a family” with an average rating of 7.2 closely followed by “experiencing a close bond between myself and my child” with an average rating of 7.0. The lowest rated items were “providing my parents with grandchildren” (average rating of 4.5) and “feeling more complete as a woman through having a baby” (average rating of 4.0). The complete list of average ratings is given in Table 6.
**Table 6. Ratings of Desirability.** Participants were asked to rate the desirability of the following categories on a scale of 0 (least desirable) to 10 (most desirable). Average ratings were computed and sorted.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Having a Family</td>
<td>7.16 (3.68)</td>
</tr>
<tr>
<td>Experiencing a close bond between myself and my child</td>
<td>6.99 (3.61)</td>
</tr>
<tr>
<td>Guiding and teaching my child</td>
<td>6.99 (3.55)</td>
</tr>
<tr>
<td>Seeing my baby’s own personality emerge</td>
<td>6.64 (3.71)</td>
</tr>
<tr>
<td>Holding and cuddling a baby</td>
<td>6.09 (3.71)</td>
</tr>
<tr>
<td>Devoting myself to raising children and being a mother</td>
<td>5.94 (3.96)</td>
</tr>
<tr>
<td>Having a son or a daughter</td>
<td>5.76 (3.88)</td>
</tr>
<tr>
<td>Being physically connected to my baby for 9 months</td>
<td>5.43 (3.74)</td>
</tr>
<tr>
<td>Being able to get pregnant</td>
<td>5.34 (3.89)</td>
</tr>
<tr>
<td>Giving my partner the satisfaction of being a parent</td>
<td>5.31 (3.75)</td>
</tr>
<tr>
<td>Feeling a baby move and kick inside me</td>
<td>5.27 (3.75)</td>
</tr>
<tr>
<td>Seeing family resemblance</td>
<td>5.20 (3.71)</td>
</tr>
<tr>
<td>Giving birth to a baby</td>
<td>4.86 (4.03)</td>
</tr>
<tr>
<td>Having companionship through a child</td>
<td>4.86 (3.50)</td>
</tr>
<tr>
<td>Breastfeeding a baby</td>
<td>4.85 (3.79)</td>
</tr>
<tr>
<td>Having a child who will carry out my family tradition</td>
<td>4.64 (3.62)</td>
</tr>
<tr>
<td>Providing my parents with grandchildren</td>
<td>4.53 (3.62)</td>
</tr>
<tr>
<td>Feeling more complete as a woman through having a baby</td>
<td>4.00 (3.84)</td>
</tr>
</tbody>
</table>
In addition to rating desirable items, participants were asked to rate the “undesirability” of seventeen items on a scale of 0 to 10, with 10 being the most undesirable score. As before, ratings for these items were not mutually exclusive. On average, the most undesirable item was having a “child with a genetic disease” with a rating of 8.9. The second most undesirable item was “having a baby who is born deformed” with a rating of 8.9. The least undesirable items (items that women were not as concerned about) were “feeling responsible for another person’s life” and “being kept away from a career by a child” with ratings of 3.7 and 4.0 respectively. The most undesirable items tended to center around having a child with poor health or leaving a child without a parent. The full list of ratings is given in Table 7.
Table 7. Ratings of Undesirability. Participants were asked to rate the undesirability of the following categories on a scale of 0 (least undesirable) to 10 (most undesirable). Average ratings were computed and sorted.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Having a child with a genetic disease</td>
<td>8.93 (2.11)</td>
</tr>
<tr>
<td>Having a baby who is born deformed</td>
<td>8.91 (2.12)</td>
</tr>
<tr>
<td>Worrying about effects of chemo/radiation on embryo formation</td>
<td>8.77 (2.11)</td>
</tr>
<tr>
<td>Becoming pregnant during a recurrence</td>
<td>8.71 (2.35)</td>
</tr>
<tr>
<td>Leaving a child behind without a parent(s)</td>
<td>8.69 (2.49)</td>
</tr>
<tr>
<td>Guilt of possibly leaving a child</td>
<td>8.69 (2.39)</td>
</tr>
<tr>
<td>Passing off negative genetic traits or diseases</td>
<td>8.60 (2.42)</td>
</tr>
<tr>
<td>Having a baby who strains my health</td>
<td>7.19 (2.63)</td>
</tr>
<tr>
<td>Feeling guilty or inadequate as a parent</td>
<td>6.45 (3.29)</td>
</tr>
<tr>
<td>Having a child who is a burden to my partner</td>
<td>6.24 (3.42)</td>
</tr>
<tr>
<td>Burden on finances</td>
<td>5.51 (3.07)</td>
</tr>
<tr>
<td>Experiencing the pain of childbirth</td>
<td>5.31 (3.57)</td>
</tr>
<tr>
<td>Taking care of a sick child</td>
<td>5.17 (3.29)</td>
</tr>
<tr>
<td>Experiencing the discomforts of pregnancy</td>
<td>4.97 (3.44)</td>
</tr>
<tr>
<td>Having a baby who takes away my freedom to do other things</td>
<td>4.43 (3.48)</td>
</tr>
<tr>
<td>Being kept away from a career by a child</td>
<td>4.00 (3.36)</td>
</tr>
<tr>
<td>Feeling responsible for another person's life</td>
<td>3.66 (3.35)</td>
</tr>
</tbody>
</table>
DISCUSSION

General limitations of the study

The survey format of the study posed several limitations to the quantity and quality of data that could be extracted. For instance, patients completed the survey at one time after their cancer diagnosis and were asked to answer questions regarding their state of mind before their diagnosis. In particular, women were asked to recall the regularity of their menstrual cycles, their priorities regarding childbearing and family planning, and whether they had a fertility discussion. All of this data could be influenced by inaccurate memories due to the time elapsed between the time periods in question and taking the survey. It should also be noted that in some cases brain tumor causes memory impairment, and this may have led to difficulty in accurately completing the questionnaire for some patients. There was substantial nonresponse in some areas of the survey, which prevented accurate evaluation of many of the primary questions that were raised. This nonresponse may have been due to the sheer length of the survey, which consisted of 71 questions (many with multiple parts). Patients may have also felt discomfort towards portions of the survey that asked about sensitive topics, or they may have elected not to answer a question if they were unable to clearly recall information.

In addition to the length of the survey, there was also some redundancy present in the survey questions. This redundancy led to difficulty in accurately interpreting data, and necessitated the removal of some areas of interest from the
final analysis. A shorter, more succinct and targeted survey may have yielded higher response and less ambiguity.

**Effect of Cancer Treatments on Fertility**

While one of the primary goals of the study was to evaluate how cancer treatment affects the fertility of women with glioma, we were not able to answer this question with a substantial degree of confidence due to significant nonresponse in this area of the survey. It is possible that women who were not attempting to have children did not respond to questions regarding fertility, even though there was an option to indicate this on the survey. Additionally, participants were not asked to consent to a medical chart review, which prevented verification of this and other data.

We also attempted to understand infertility in our sample by the indirect means of evaluating changes in menstrual cycle. Data showed that some type of change in menstrual cycle was very common among participants, especially among those who underwent chemotherapy. While change in menstrual cycle does not necessarily indicate loss of fertility, research has shown a correlation between women who experience menstrual changes during chemotherapy and those who report infertility. The extent to which menstrual changes were reported suggests a serious risk to fertility within our sample.
**Determination of Prevalence and Effectiveness of Fertility Counseling**

Women who had not undergone chemotherapy for their tumor were less likely to report having a fertility discussion than those who had. This is consistent with the understanding that the greatest threat to fertility for brain cancer patients is chemotherapy. Targeted brain irradiation is unlikely to cause damage to distant tissues. Therefore, a physician would not necessarily need to educate their patient about possible loss of fertility if the patient was only receiving some combination of surgery or radiotherapy. Within the subset of patients who underwent chemotherapy for their brain tumor, we found that only 35% recalled having a discussion regarding fertility risks and preservation with their physician. Even taking into account the fact that this number may be low due to recall bias, this statistic is alarming. Since all common chemotherapy treatments pose a risk to fertility, any patient receiving these therapies should be given information notifying them of these risks. It is possible that physicians do broach this subject with patients, but do so when they are still recovering from the initial shock of being given a brain tumor diagnosis. If this is the case, it may be best to delay this discussion until after patients have had time to process their diagnosis and are receptive to more information regarding their tumor and possible treatments.

Interestingly, more patients reported being aware that treatments could affect their fertility than reported having a fertility discussion. This may indicate that patients are finding this information on their own using outside resources. Because outside
resources can vary in source and accuracy, they should be reinforced by information from a medical professional caring for the patient.

The survey results also indicated that 80% of those who do report having a fertility discussion are aware that treatment may affect their fertility. This result is encouraging as it demonstrates that discussions are somewhat effective and may help patients make educated choices regarding preserving their fertility prior to treatment. The 20% of women who do not report awareness despite having a fertility discussion may represent those patients for which these risks need to be reiterated.

The results also showed that the higher the grade of tumor a patient had, the more likely they were to be aware of the detrimental effects of treatment, even controlling for whether individuals underwent chemotherapy (p=0.02).

While most patients reported having a fertility preservation discussion with their oncologist, patients also indicated they would be most comfortable having this discussion with a reproductive specialist. This disparity may indicate that patients are interested in receiving more specific information regarding their fertility options, and that referrals to a reproductive specialist should be standard.

An important finding in the study was that 21 women reported that they did not bring up the topic of fertility preservation because it was not important to them at the time of diagnosis, but was important to them at the time of being surveyed. This discrepancy may be caused by many factors: patients being overwhelmed by the implications of their new diagnosis, not being aware that infertility is an issue, or
not planning on children at the time of diagnosis. The fact that the proportion of women wanting children decreases after diagnosis indicates that this is probably not the cause of the discrepancy. Instead, it is likely that patients are overwhelmed by their new diagnosis and undereducated to the risks of cancer treatment on their fertility, causing them to neglect initiating this discussion with their physician before undergoing treatment.

Priorities of Women with Glioma regarding childbearing and family planning

Results of the survey showed that women were less likely to report wanting another child after treatment than before their diagnosis. In addition, women report that health becomes more important after treatment while having children loses some importance. These results show a shift of priorities toward taking care of self versus planning for a family.

In reviewing the ratings of “desirability” and “undesirability” given to topics of family planning and childrearing, a few patterns emerge. The most highly undesirable items tend to be those that pertain to either passing health problems onto offspring or leaving children without a parent. It is unclear whether the women surveyed were concerned that their tumor may be an indicator of poor health in their children, or that treatment would affect the genetic health of their gametes. In either case, it is clear that patients have concerns regarding the health of their future offspring, and these concerns may be addressed in a comprehensive fertility discussion. The worry of leaving a child without a parent may explain some of the
decrease in desire to have children after tumor treatment as opposed to prior to diagnosis.

**Suggestions Going Forward**

Suggestions for clinicians are based on the principal results of this study:

- Only 35% of women receiving chemotherapy for their glioma recall having had a conversation regarding fertility preservation prior to initiating treatment.
- Only 80% of those who had a fertility preservation discussion reported awareness that treatment could affect their fertility.
- A substantial proportion of respondents reported that while fertility preservation was not important to them at the time of diagnosis, it was important to them at a later date.
- Most women surveyed desired to speak with a reproductive specialist about fertility preservation methods.

These data suggest a lack of knowledge from women undergoing cytotoxic chemotherapy for their brain tumor in regards to the hazards of this therapy on their reproductive health. Furthermore, the results of this survey suggest that patients who do have fertility preservation discussions with their doctors may still be left with gaps in their understanding. We suggest that a fertility preservation discussion be initiated with a patient that is considering chemotherapy before treatment begins. It may be best to broach this topic with patients after the initial shock of their brain tumor diagnosis subsides in order to increase retention.
However, in the setting of a brain tumor diagnosis, immediate treatment is often fundamental to prolonging survival. Therefore, it may not be feasible in many cases for physicians to have this discussion with their patients at a later date. It may also be helpful to have this conversation in the presence of the patient’s caregiver (spouse or family member) if they are available.

It may also be in the patient’s best interest to offer a referral to a reproductive specialist so that patients may gain a complete understanding of the risks to their fertility and their options to circumvent this risk. However, insurance may not pay for a consultation with a fertility expert, let alone fertility preservation procedures themselves. These are all issues that must be assessed on a case-by-case basis taking into account the patient’s priorities and the healthcare available to them.

We believe that this survey itself increased awareness of fertility issues among neuro-oncologists at our institution (University of California, San Francisco). In addition, the field of neuro-oncology is evolving to encompass issues of fertility and of quality of life after tumor treatment due to the increased life expectancy of patients in the last decade. These changes in the field may lead to an improvement in fertility outcomes and general quality of life of brain cancer patients in the future.
REFERENCES


CURRICULUM VITAE

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Email: rstiner@bu.edu • Year of Birth: 1990

EDUCATION

Boston University
M.S., Medical Science
Boston, MA
Expected Graduation May 2016

University of California, Berkeley
B.A., Integrative Biology
Berkeley, CA
Graduated May 2012

RESEARCH AND CLINICAL EXPERIENCE

University of California, San Francisco
Clinical Research Coordinator, Neuro-oncology
San Francisco, CA
June 2015 - Present
• Manage data for a large portfolio of clinical trials in neuro-oncology, encompassing both pharmaceutical trials and investigator-initiated studies.
• Work with study physicians and nurses to prepare for upcoming trials as well as ensure compliance of current protocols.
• Collaborate with sponsor representatives to ensure data quality and completeness.
• Perform statistical analyses of both retrospective and prospective clinical studies and prepare manuscripts for publication.

University of California, San Francisco
Clinical Research Coordinator, Pulmonology
San Francisco, CA
June 2013 - May 2014
• Managed three clinical pulmonary studies: composed and modified study protocols, worked with IRB and study sponsors, and recruited, screened, and consented study participants.
• Cultured human alveolar macrophages, performed phagocytosis assays utilizing Jurkat cell line, and analyzed results using fluorescence microscopy and computational imaging.
• Performed data analysis using STATA and Microsoft Excel, presented results at team meetings and modified study and experiment protocols as necessary.

Siemens Healthcare Diagnostics
Microbiologist, Process Engineering
Sacramento, CA
June 2012 – May 2013
• Performed rigorous quality control tests on marketed diagnostic health products.
• Utilized chemical (spectrophotometric and HPLC) and biological (minimum inhibitory concentration) assays to analyze purity of raw materials used in
diagnostic health products.

- Evaluated quality of raw materials from potential new suppliers and authored reports of test findings and recommendation of approval or rejection.

**Ellen Simms Laboratory**

Research Assistant

Berkeley, CA

Jan 2010 – May 2012

- Designed and implemented chemotaxis assays examining symbiosis between nostacaelean cyanobacteria and hornworts; measured and recorded frequency of preferential symbiosis; analyzed data using SPSS.
- Performed DNA extraction and PCR in order to identify bacterial species.
- Maintained bacterial cultures and hornwort colonies: subcultured, refreshed media, and modified incubation conditions as necessary.

**USDA Human Nutrition Research Center**

Research Assistant

Davis, CA

June 2007 – Sept 2007

- Researched carotenoid extraction methods from primary sources and synthesized into project proposal.
- Executed extraction protocol using high-performance liquid chromatography (HPLC) and column chromatography.
- Presented experimental design and results in both written report and research symposium.

**ADDITIONAL EXPERIENCE**

**Cal Habitat for Humanity**

Volunteer

Berkeley, Chile

August 2008 - May 2012

- Built homes alongside low-income residents of Alameda County and participated in community service activities directed toward helping residents attain housing.
- Constructed homes in a Navajo community in Northern Arizona, helping to rebuild an underserved community that had experienced severe hardships.

**Escuela El Monte**

Career Preparation Instructor

Santiago, Chile

July 2011 - Dec 2011

- Designed career preparation curriculum for special needs students in rural suburb of Santiago, Chile
- Implemented curriculum which included basic math, writing, and public speaking; allowing students to gain skills and confidence in practical areas

**East Bay Sanctuary Covenant**

Intake Volunteer

Berkeley, CA

Aug 2009 - May 2011

- Gathered history immigrants seeking political asylum and synthesized into report for covenant legal counsel.
- Translated documents from Spanish to English for legal aides.

**People’s Test Preparation Services**

Verbal Teaching Coordinator

Berkeley, CA

Dec 2010 - May 2011

- Taught 2-unit course for SAT tutors, preparing tutors to teach weekly classes.
- Redesigned outdated curriculum, improving quality of lessons and increasing student retention.
- Led workshops focusing on public speaking, classroom preparation and lesson planning.

**People's Test Preparation Services**

Berkeley, CA

**SAT Instructor**

Aug 2009 - May 2011

- Facilitated free semester-long SAT preparation courses in Oakland, CA and Berkeley, CA.
- Provided one-on-one feedback to students on SAT essays and college personal statements.
- Conducted workshops on college admission and individual SAT subject tests.

**Hobbies:** guitar, running, biking, weightlifting, creating and building electronics, baking, improv, reading, nutrition and fitness, freelance translation