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A Mathematical Survivor Function Model for Predicting the Effects of Cancer Treatment on Ovarian Function

S. Lakshmi [1], Akanksha A. Desai [2]
[1] Research Advisor, Department of Mathematics, Kunthavai Nachiyaar Government Arts College for Women(Autonomous), Thanjavur/ Bharathidasan University, India
[2] Research Scholar/ Bharathidasan University, India

ABSTRACT:

To predict the age at which ovarian failure is likely to develop after radiation to a field that includes the ovary in women treated for cancer. The dose tolerance of the ovary is dependent on several factors including the volume irradiated, the total radiation dose, the fractionation schedule and the patient's age at the time of treatment. Here we have developed a mathematical survivor function model for predicting the age of ovarian failure compared with more follicles.

Keywords— *Ovarian failure , Chemotherapy, Irradiation, Radiation Dose Tolerance, Ovarian Function.*

I. INTRODUCTION

Cancer Treatments in Ovary

Over the last few decades, the prognosis of patients with cancer has dramatically improved. The long-term consequences of cancer treatment on patients with cancer have dramatically improved. The long term consequences of cancer treatment on patient's quality of life have become a major issue. Premature ovarian failure is an established long term adverse event of cancer treatments and has a significant impact on quality of life in young patients. However increasing numbers of survivors are now confronted with the long term consequences of exposure to these treatments. Cancer treatment includes surgery, radiotherapy and chemotherapy can have a profound impact on ovarian function, leading to premature menopause and loss of fertility.

II. TREATMENT METHODS

2.1. Radiotherapy & Chemotherapy

Radiotherapy is therapy using ionizing radiation, generally as part of cancer treatment to control or kill malignant cells. Radio therapy is synergistic with chemotherapy and has been used before during and after chemotherapy in susceptible cancers. Ionizing radiation works by damaging the DNA of cancerous tissue leading to cellular death. To spare normal tissues shaped radiation beams are aim from several angles of exposure to intersect at the tumor, providing a much larger absorbed dose there than in the surrounding healthy tissue. Radiation oncology is the medical specialty concerned with prescribing radiation and is distinct from radiology, the use of radiation in medical imaging and diagnosis.[7]

Chemotherapy is a category of cancer treatment that uses chemical substances especially one or more anti cancer drugs that are given as part of a standardized chemotherapy regimen. Chemotherapy may be given with a curative intent or it may aim to prolong life or to reduce symptoms. Importantly, the use of drugs (whether chemotherapy, hormonal therapy or targeted therapy) constitutes "systemic therapy" for cancer in that they are introduced into the blood stream and are therefore in principle able to address cancer at any anatomic location in the body. Systemic therapy is often used in conjunction with other modalities that constitute "local therapy"(i.e. treatments whose effecting is confined to the anatomic area where they are applied) for cancer such as radiation therapy, surgery and /or hyperthermia therapy.

2.2 Ovarian Failure

Acute ovarian failure can occur during or shortly after completion of irradiation or chemotherapy and may be transient or permanent .In contrast, premature ovarian failure(POF) or premature menopause typically manifests after a post treatment return of regular menses with subsequent loss of ovarian function before the age of 40 years. As expected , surgical ablation of the ovaries leads to immediate and permanent loss of function.[10]

2.3 Toxic Effects

The toxic effects of radiation therapy on ovarian function have been well documented. Ovarian tolerance is a function of the number of remaining primordial follicles, which is related to age, younger patients have more follicles and therefore require higher doses of radiation to ablate ovarian function. The human oocyte is radiosensitive with a low LD_{50} approximately 2 Gy. The models assist the physician in predicting the age of ovarian failure after treatment with a known dose of radiation.

The effective (upper) and mean (lower) sterilization dose of a radiation for a given treatment age.[4]

Medical Figure

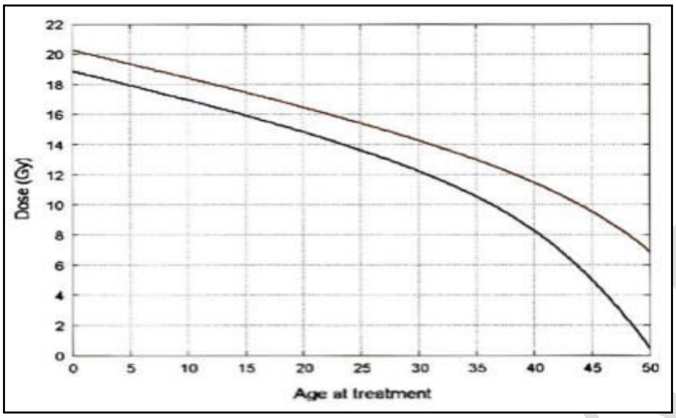
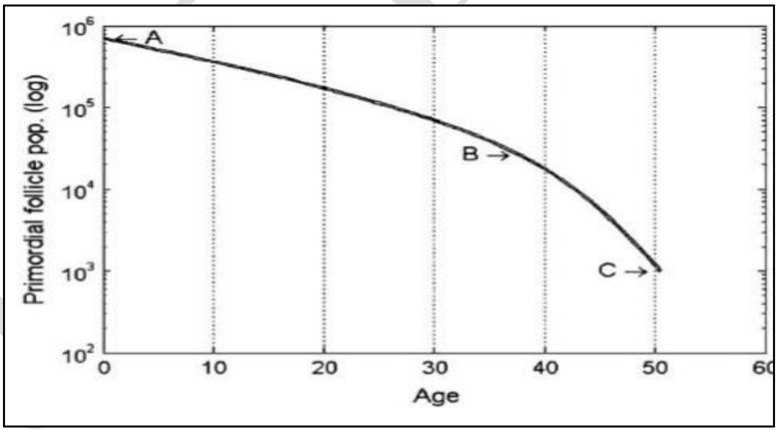


Fig A. Dose Radiation Therapy

Early estimation of the age of ovarian failure will help physicians manage young female patients from puberty through premature menopause with appropriate timing of HT and discussion of available fertility preservation options.

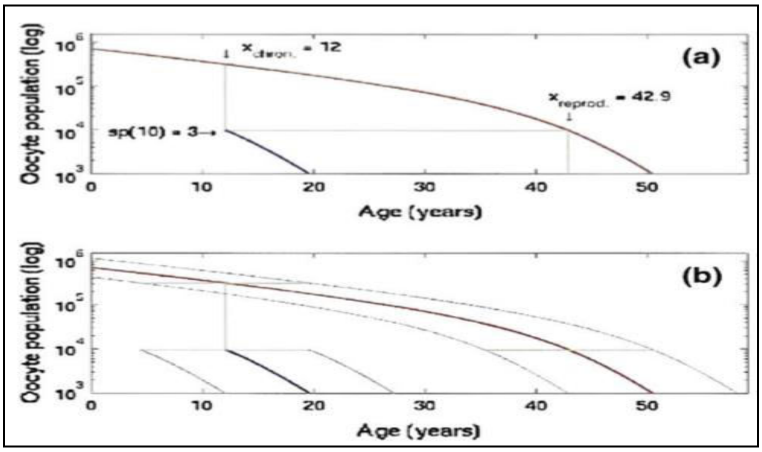
2.4 **Solution of the Faddy-Gosden Differential Equation for The Primordial Follicle Population from Birth to Menopause**

Fig 1 The solution of the Faddy-Gosden differential equation for the primordial follicle population from birth to menopause[2]



(A) At birth, 701,000 follicles.
(B) Accelerated decline at age 38 yrs, 25,000 follicles.
C} At menopause, 1000 follicles [2]

Figure 2. Model for predicting the Ovarian Failure after Radiotherapy



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For a given dose of radiotherapy at a known chrono-logic age (X_{chron}) (Fig. 1), the surviving fraction of oocytes and thus the age of ovarian failure can be determined .The solution to the Faddy-Gosden equation and the surviving percentage function. An example of the method for predicting ovarian failure after a 12-year-old girl receives a dose of 10 Gy to the ovaries is shown in Figure 2. Using the model, the average population at an age of 12 years (x_{chron}) is 312,000 follicles. After 10-Gy ovarian irradiation, the surviving percentage is $\log_{10}$ g (10) = 3.01%, corresponding to a population of 9,600 follicles. Projecting that number of remaining follicles onto the standard Faddy-Gosden model reveals a reproductive age (X_{reprod}) of 42.9 years. The average 42.9-year-old woman is expected to experience menopause in 7.5 years, at an age of 50.4 years. The patient's predicted reproductive lifespan is therefore 50.4 — X_{reprod} years. Her predicted age of ovarian failure is x_{chron} + (50.4 — Xr_{eprod}) years or 12 + (50.4 — 42.9) = 19.5 years. The predicted age of ovarian failure for patients from birth to 30 years old at the time of treatment and for ovarian doses of 3, 6, 9, and 12 Gy.[1]

III. MATHEMATICAL MODEL FOR SURVIVOR FUNCTION

Let T be a discrete random variable that takes the values $t_1<t_2<\ldots$ with probabilities

$$f(t_j) = f_j = \Pr\{T = t_j\}.$$

We define the survivor function at time tj as the probability that the survival time T is at least t_j

$$S(t_j) = S_j = \Pr\{T \geq t_j\} = \sum_{k=j}^{\infty} f_j.$$

Next , we define the hazard at time t_j, as the conditional probability of dying at that time given that one has survived to that point, so that

$$\lambda(t_j) = \lambda_j = \Pr\{T = t_j | T \geq t_j\} = \frac{f_j}{S_j}.$$

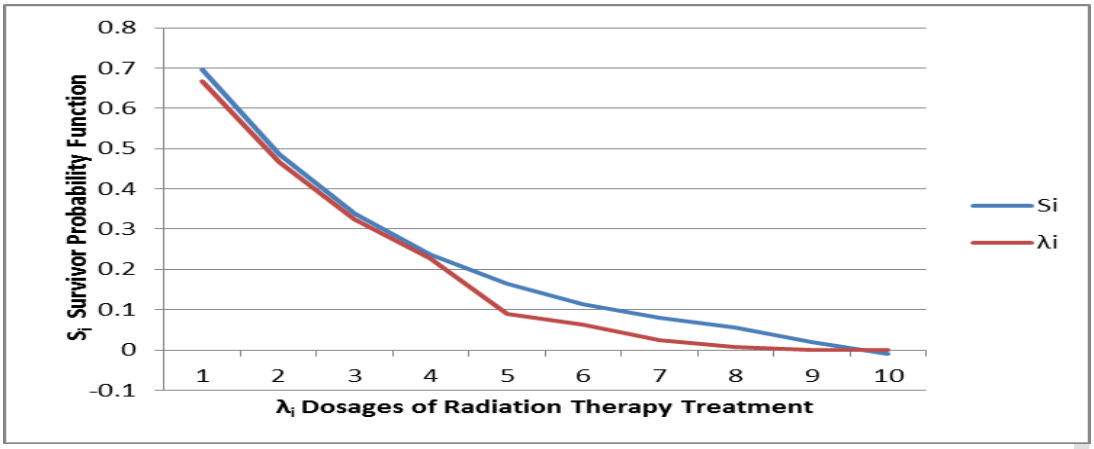
Note that in discrete time the hazard is a conditional probability rather than a rate. However, the general result expressing the hazard as a ratio of the density to the survival function is still valid.[6]

A further result of interest in discrete time is that the survival function at time t_j can be written in terms of the hazard at all prior times $t_1,\ldots,t_{j-1}$ as

$$S_j = (1-\lambda_1)(1-\lambda_2)\ldots(1-\lambda_{j-1}).$$

In words, this result states that order to survive to time t_j one must first survive t_1, then one must survive t_2 given that one survived t_1, and so on, finally surviving t_{j-1} given survival up to that point. This result is analogous to the result linking the survival function in continuous time to the integrated or cumulative hazard at all previous times.[8]

MATHEMATICAL FIGURE



Where λ_i is the conditional probability in the i-th interval of age for the sterilizing dose of radiation and S_i is the survivor probability function for the corresponding λ_i.. Upper curve denotes survivor function when the effective sterilizing dosages of radiation is given and it is continuous monotonic decreasing curve.[3] Lower curve denotes survivor function when the mean sterilizing dosage of radiation is given and also it is continuous monotonic decreasing curve.[5]

CONCLUSION

Recent advances in cancer therapy has resulted in increasing numbers of long term survivors who are then left to deal with consequences of their treatment. The sensitivity of the ovaries to irradiation and chemotherapy often results in impaired fertility and premature menopause. More effective mathematical survivor function models are needed for predicting age of ovarian failure after a known dose of radiotherapy. In this direction here we have developed a mathematical survivor function model for predicting the age of ovarian failure compared with more follicles.[8]

From the mathematical survivor function decreases from the age of 30 years to 50 years (till menopause) in both the cases of effective and mean sterilizing dosage of irradiation in the mathematical model there in a difference in the survivor function after the age of 30 years and the curve decreases suddenly when in case of mean sterilizing dose of radiation in given. So treating physician should take an active role in both reducing potential ovarian toxicity in every way possible and in providing the means where by the patient can make an informed decision regarding her options for fertility preservation. Radiation doses more than 24 Gy will produce permanent ovarian ablation .Although most fertility options are still considered experimental with efficacy and reliability yet to be determined the future of fertility preservation for females cancer survivors is promising.[9]

REFERENCES

[1] Bleyer WA. The impact of childhood cancer on the United states and the world. CA Cancer J Clin 1990;40:355-67
[2] Cawley,G.C.,B.L.C. Talbot,G.J.Janacek,and M.W.Peck.2006.Sparse Bayesian Kernel Survival Analysis for Modeling.
[3] Cox,D.R and D.Oakes 1984. Analysis of Survival Data. Chapman and Hall.London.
[4] Gook DA, Edgar DH. Human oocyte cryopreservation. Human Report Update 2007;13-591-605.
[5] Hosmer D.W.,Lemeshow S., and May S.,Applied Survival Analysis : Regression Modeling of Time-to-Event Data,Wiley,2008.
[6] Klienbaum D.G., Survival Analysis, a self learning text , Springer-Verlag,1996.
[7] Monnier A. Clinical management of adverse events in adjustment therapy for hormone responsive early breast cancer. Ann Oncol 2007;18(suppl)viii36-44.
[8] Pena,E.A. and E.H.Slate 2005. Dynamic modeling in reliability and survival analysis. In “Modern Statistical and Mathematical Models in Reliability. Edited by A.Wilson,N.Limnios,S.Kelly-Mc Nulty,Y.Armijo.pp.55-71.
[9] Wallace WH, Kelsey TW. Ovarian and reproductive age may be determined from measurement of ovarian volume by transvaginalsonography. Hum report 2004;19:1612-7
[10] Wallace WH, shalet SM, Hendry JH, Morris-Jones PH, Gattamaneni HR. Ovarian failure following abdominal irradiation in childhood: the radiosensitivity of the human oocyte. Br J Radiol 1989;62:995-8