

Pregnancy and Radiotherapy: Protecting Fetuses from the Effects of Radiation

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Abstract

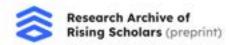
Some pregnant women have cancer and need to receive radiotherapy treatment. However, radiotherapy can be dangerous, especially for the fetus. Radiation exposure can cause many harmful effects on the fetus, including potential death, growth impairments, and many neurological effects like mental retardation, severe intellectual disability, brain injury, loss of IQ points, and more. Such symptoms can hinder the offspring's ability to succeed later on in life after birth. Pregnant women who require radiotherapy often have to compromise between their health and the health of their child. Making radiotherapy safer and finding ways to treat already existing radiation exposure symptoms in fetuses is extremely important. Pregnant patients should feel confident in the safety and effectiveness of their treatment and should not have to choose between their health and the health of their child. The objective of the research is to find methods to increase the safety of radiotherapy, especially when it comes to protecting the fetus from the effects of radiation exposure, and also find ways to treat already existing symptoms of radiotherapy.

Introduction

Imagine someone is going to be a mother. Imagine someone is pregnant and is expecting a child. However, they also have cancer and need to receive radiotherapy treatment for it. A radiation dose of one Grey (Gy), which is defined as absorption of 1 joule of radiation energy per kilogram of matter, can kill 50% of embryos, and a dose of five Gy can kill 100% of embryos within 18 weeks. Such a small amount of radiation can be fatal to developing fetuses, and radiotherapy is a type of cancer treatment that relies on ionizing radiation. Even if radiotherapy does not result in the death of embryos, it still has many side effects that hinder the development of future individuals. Some of the side effects include mental retardation, impaired visual function, neurological injury, and loss of IQ points. A decrease in IQ points increases the risk of severe intellectual disability. The mother is torn between choosing her health or the well-being of her future offspring. What if she could have both? What if professionals could refine radiotherapy so it is safer for the patient's future child? Radiotherapy can be improved by utilizing particular devices and treatments, implementing aspects of other treatments into radiotherapy, creating strict regulations for radiotherapy procedures, and tailoring treatment for pregnant individuals. The purpose of the paper is to inform the reader how radiotherapy can be improved when treating pregnant patients to prevent harmful effects on the fetus. The paper will discuss how each of these ideas will upgrade the safety of radiotherapy.

Devices and Treatments

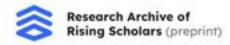
Professionals can use various medical devices and treatments during radiotherapy to protect the patient and the fetus from radiation or cure radiation-induced injury. One device is the Scale Mail



Armor for Radiation Therapy (SMART). SMART armor is made up of scale mail, which reduces radiation exposure to the breast area during radiotherapy for breast cancer (Butson, 2017). Macinely Butson, the inventor, created the device by interweaving scales with copper because she found it more effective than lead for shielding. The use of SMART armor demonstrated a reduction in radiation exposure by up to 80% (Butson, 2017). The Food and Drug Administration (FDA) approved the invention, meaning that it fits the standard of being safe and effective. Professionals can remodel SMART armor for pregnant patients to protect the region of the fetus. The use of SMART armor will reduce the amount of exposure the fetus receives during treatment. Another medical procedure that can benefit the fetus is the intranasal administration of human mesenchymal stem cells (hMSCs). An experiment conducted on mice reveals that hMSCs effectively repair brain injury and improve brain function without posing risks to the lives of mice with glioma, a malignant tumor of the glial tissue of the nervous system. It also protects against inflammation, oxidative stress, and neuronal loss (Soria et al., 2019). Because the hMSCs are effective in mice, they will likely benefit humans since mice are genetically similar to humans. Professionals can administer hMSCs to newborn babies that were affected by radiotherapy exposure. Doing so will treat any neurological injuries and will reduce the chances of the baby growing up with any mental disabilities. hMSCs should exist in the treatment room as a backup in case the fetus experiences neurological harm from radiotherapy treatment. Another backup treatment is hyperbaric oxygen treatment (HBOT). A study exploring the effects of HBOT revealed that the symptoms of all the tested patients were either improved or stabilized after the experiment (Chuba et al., 2000). Although the patients exhibited no severe side effects related to HBOT, four patients ended up dying because of tumor progression. Even though HBOT is not perfect for treating neurological symptoms, it demonstrated improvement in the patient's condition. Volumetric modulated arc therapy (VMAT) and image-guided radiotherapy serve a benefit also. Techniques like VMAT arcs and image-guided radiotherapy provide precise dose conformation to target volumes while minimizing radiation exposure to surrounding healthy tissues (Sergieva et al., 2023). The techniques contribute to reduced toxicity and improved long-term cure rates. VMAT arcs and image-guided radiotherapy enable personalized treatments based on clinical and anatomical parameters, thus contributing to higher survival rates and improved quality of life for patients (Sergieva et al., 2023). Using these techniques will make radiotherapy treatment safer for the pregnant patient and the fetus.

Aspects of Other Treatments

Another way radiotherapy can be made safer is by implementing aspects of other types of treatments into radiotherapy. One of those treatments is Tumor Treating Fields. Tumor Treating Fields use low-intensity electric fields to treat cancer. Electric fields differ from electric currents, ionizing radiation, or magnetism and act as a force on objects with electrical charges (Doyle, 2012). In cancer, the fields interfere with the division of rapidly multiplying cells by stopping the formation of vital protein chains. Tumor Treating Fields pass through transducers attached to a field generator that creates an artificial electrical field around cancer cells, and the procedure disrupts the division process and kills or ceases the formation of unhealthy daughter cells. The fields do not affect normal non-dividing cells. Tumor Treating Fields are incredibly efficient in treating cancer. A study reveals how a patient with Glioblastoma multiforme (GBM) experienced tumor regression and longer life expectancy due to Tumor Treating Fields therapy. Also, clinical trials proved that Tumor Treating Fields can extend survival without the side effects caused by



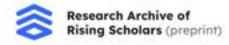
chemotherapy (Doyle, 2012). Not only are tumor treatment fields effective, but they are also much safer than standard chemotherapy and radiotherapy treatments. If professionals use low-intensity electric fields during radiotherapy treatment, the fetus will be less likely to develop the harmful side effects of regular radiotherapy. Also, doctors can administer various chemotherapy drugs after organogenesis, a phase of embryonic development, for up to three weeks before the patient gives birth (Schwab et al., 2023). Although chemotherapy itself as a treatment can be harmful to the patient, not to mention the fetus, administering some chemotherapy drugs during a specific phase of pregnancy decreases the chance of the drugs harming the fetus.

Regulations for Radiotherapy

It is also vital that there are strict regulations put in place for radiotherapy treatment procedures to ensure the safety of both the patient and the fetus. Professionals should apply the principles of "Time-Distance-Shielding" to reduce exposure (Lakhwani et al., 2018). The principles are: reduction of exposure time, increased distance from the radiation source, and proper shielding from radiation. Medical doctors treating pregnant radiotherapy patients should strictly follow "Time-Distance-Shielding" principles so that the treatment is as safe as possible. Furthermore, organs like the thyroid, breasts, and gonads should be protected during treatment (Lakhwani et al., 2018). Not only is it crucial to provide shielding, but professionals must ensure the protection of vital organs to avoid damage. The belly should especially be protected, considering that is where the fetus is. Regulations should be in place requiring essential areas to be covered. In addition, doctors need to ensure that the protection devices they use shield the patient and the fetus effectively from radiation. Unfortunately, there may be cases where such precautions might not successfully protect the fetus from radiation. There is no one-size-fits-all approach, and some fetuses might be more vulnerable to radiation-induced harm than others. In these instances, professionals should conduct radiotherapy treatment post-delivery (Schwab et al., 2023). Radiotherapy should be avoided during iatrogenic preterm delivery because it is a significant risk factor for long-term impacts on the child (Schwab et al., 2023). It is best to delay treatment after the patient gives birth and is no longer carrying the child inside of her. If the patient urgently needs to receive radiotherapy and cannot wait until post-delivery, surgery during pregnancy is a possible option, preferably during the second trimester of pregnancy (Schwab et al., 2023). Of course, there should be regulations for that as well. Professionals should closely examine the condition and the fetus and effectively determine the best course of action. If they decide that surgery during pregnancy is the way to go, doctors should make sure they do the surgery adequately and during the appropriate stage of pregnancy. It is also necessary that the regulations are direct and clear so that there is no confusion about how to follow them. Creating and enforcing proper treatment regulations is crucial in ensuring the safety of pregnant patients and their fetuses.

Specialized Treatment

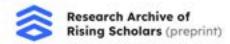
As mentioned before, there is no one-size-fits-all approach to radiotherapy treatment, especially during pregnancy. Radiotherapy treatment should be tailored for pregnant patients to benefit the mother and the fetus. Professionals should adjust it by regulating the radiation dosage and treatment based on the patient's condition. Professionals can minimize the dose by delaying radiotherapy treatment until a later stage of pregnancy, calculating the needed dosage before



the patient undergoes treatment, and modifying the treatment plan to ensure the fetus receives less radiation exposure (IAEA, 2023). Medical professionals should regulate such factors depending on the urgency of treatment and the sensitivity of the mother and the fetus. The type of cancer, its stage, biology, and timing of diagnosis are critical factors to consider (Schwab et al., 2023). Each type of cancer varies in severity and treatment needs, so doctors should adjust treatment plans based on the type of cancer diagnosis of the patient. Doctors should manage cancer treatment during pregnancy to benefit the overall well-being of the mother and the offspring (Ring et al., 2005). Doctors should find a method of cancer treatment that does not require sacrificing an individual's health for the health of their child. Radiotherapy treatment must be safe and beneficial for both the patient and her fetus. Visual assessments are a good way for professionals to decide the treatment plan for pregnant individuals. One study concludes that recognizing visual impairments is crucial for early intervention programs to protect or improve the visual and developmental outcomes of preterm infants (Ramenghi et al., 2010). Visual assessments help recognize visual impairments of fetuses. Analyzing a fetus' current brain health will help decide the optimal treatment procedure. Visual assessments will aid doctors in determining the sensitivity of the fetus. If the fetus is in bad condition before the treatment, professionals will know that they need to further restrict the amount of radiation exposure. Knowing the sensitivity will also help patients decide how long they should wait to receive treatment or if they should receive it all based on their needs. Analyzing visual assessments and neuroimaging in newborns provides valuable information regarding the relationship between brain structure and function in early life, which is necessary for cognitive development. (Ramenghi et al., 2010). Visual assessments are beneficial in providing insightful information on a fetus' or newborn's brain health. Furthermore, they are advantageous in analyzing the neurological development of fetuses, thus helping to determine the amount of sensitivity regarding radiation exposure. Radiotherapy treatment must be specialized for each patient with the help of visual assessments and other methods to ensure the best possible outcome for the patient and her child.

Primary Research and Analysis

Although the literature review provided insight into ways to improve radiotherapy safety for fetuses, primary research was necessary to build off the data and analyze more intricate effects of radiotherapy-related treatments. The sources included literature review only offered summaries of studies, whereas a more thorough analysis would allow for a deeper glimpse into more specific and exact data. An in-depth primary analysis would reveal the specific conditions for a particular result, variations among experimental outcomes, and other factors. For primary research, four articles were reviewed for a meta-analysis. Each of the data tables from the articles are located in the appendix. The articles used for the primary meta-analysis are "WHO Framework for strengthening and scaling-up services for the management of invasive cervical cancer," "Radioprotectors and Radiomitigators for Improving Radiation Therapy: The Small Business Innovation Research (SBIR) Gateway for Accelerating Clinical Translation," "Brochure for Physicians: Prenatal Radiation Exposure," and "Advances in Radiotherapy." The data from each of the articles is recorded in Table 1, Table 2, Table 3, and Table 4, respectively. The overall



findings from each table are recorded in Table 5. Although the articles each focus on different aspects of radiotherapy, they all reveal crucial information about making radiotherapy safer. A meta-analysis was the most appropriate form of primary research since there was no access to lab equipment or radiotherapy-related drugs or devices to conduct an experiment and analyze detailed observations. However, using previously existing data from past experiments has allowed for the observation of various radiotherapy treatments without needing to run an experiment. The data from Table 4 demonstrates that radiotherapy is vital for treating various types of cancer and is effective. The table includes data on various cancer treatments for different kinds of cancer. The table also records the results of each

Summary of radiotherapy interventions in the management of cervical cancer

Intervention	Abbreviation	Procedure	Intent/advantage	Associated risks/ adverse events
External beam radiotherapy	EBRT	Radiotherapy delivered from a distance.	Curative for small to large lesions in combination with BT and chemotherapy. Palliative to control bleeding and/or pain.	Infertility Menopause Vaginal dryness Bowel, urinary, haematological and skin toxicity
Brachytherapy	BT	Radiotherapy delivered from a sealed radioactive source placed inside the vagina and uterus, close to the tumour.	Curative for small to large lesions in combination with EBRT.	Vaginal stenosis; vaginal dryness Radiation proctitis Bowel and bladder toxicity May require anaesthesia
Adjuvant radiotherapy	aRT	EBRT and/or BT administered after surgery.	> Eradication of any microscopic disease in the irradiated area.	> Bowel, urinary, haematological and skin toxicity

Table 1. Summary of radiotherapy interventions in the management of cervical cancer (From WHO Report (2020), [14]).

treatment depending on what it treated. Many of the treatments used have demonstrated a reduction in the risk of death and other cancer-related effects. Table 1 reveals the advantages of different types of radiotherapy. Some of the benefits are that radiotherapy is curative to small and large lesions, palliative to control bleeding and pain, and can eradicate microscopic diseases in irradiated areas. Professionals cannot completely ignore radiotherapy in cases of pregnancy. Radiotherapy is vital for treating cancer patients. However, the findings from the primary meta-analysis also prove that radiotherapy can pose serious safety and health risks. The same data listing the advantages of different types of radiotherapy also describes the risks of those treatments. Among the potential side effects are skin toxicity, future infertility.



Summary of Activities in the Radioprotectors and Radiomitigators Portfolio

Indication	Drug; company	Award type	Year started	Current	Model	Aims
Enteritis	DFMO (α- difluoromethylomithine); RxBio Inc., Johnson City, TN	Phase I	2011	Complete	Mouse model of pelvis irradiation; HCT116 and H29 cell lines; and mouse model of colon cancer.	Evaluate radioprotecting/ radiomitigating effect on gastrointestinal injury. Evaluate the effect on cancer radiosensitivity.
Enteritis	ABC294640 (sphingosine kinase inhibitor); Apogee Biotechnology Corp., Hummelstown, PA	Phase I	2014	Ongoing	In vitro cell lines; mouse model of gastrointestinal acute radiation syndrome.	Perform proof-of-concept studies to show that drug will reduce GI-ARS following abdominal or pelvic radiation.
Proctitis	PAAG-ployglucosamine; Synedgen, Claremont, CA	Phase I	2014	Ongoing	Rat, acute radiation- induced proctitis.	Demonstrate efficacy in mitigation of radiation- induced proctitis. Develop plans to demonstrate that PAAG does not protect cancer cells during radiotherapy.
Mucositis	CBLB502 (TLR-5 agonist); Buffalo Biolabs, Buffalo, NY	Phase I	2012	Complete	Mouse model of head and neck cancer.	 Demonstrate protective effect to skin and oral mucosa after single- and fractionated multiple radiation dose regimens. Demonstrate safety and efficacy of the drug in combination with radiotherapy.
Mucositis	RLIP76 (proteoliposome); Terapio Inc., Austin, TX	Phase I	2013	Complete	Hamster cheek.	 Develop RLIP as a topical mouthwash. Test efficacy, systemic absorption and demonstrat no tumor protection.
Mucositis	JVRSOD (gene therapeutic); Colby Pharmaceuticals, Menlo Park, CA	Fast track	2013	Ongoing	Mouse model and patients with head and neck cancer.	Perform dose- and schedule- optimization studies for protection from radiation-induced oral mucositis. Identify and qualify a GMP manufacturing site. Submit an IND application for JVRSOD. Perform phase I safety and phase II efficacy clinical trials.
Mucositis	BMX-001 st (metalloporphyrin antioxidant); BioMimetix JV, Engelwood, CO	Phase I	2014	Ongoing	Mouse model of head and neck squaenous cell carcinoma.	 Establish optimum dose schedule to reduce xerostomia and mucositis. Demonstrate that the drug does not interfere with standard of care.
Lung injury	UTL-5g (TNF-2 modulator); 21st Century Therapeutics Inc., Detroit, MI	Phase I	2011	Complete	Cell lines and mouse model of lung injury.	 Examine whether the drug reduces tumor cell killing in vitro. Demonstrate efficacy in reducing radiation-induced lung injury in vivo. Demonstrate that the drug does not affect tumor cell killing induced by radiation in vivo.

Continued on next page

Whether the drug protects also

cancer stem cells or whether

its protective effects are

demonstrate safety.

ratio.

studies.

Perform preclinical studies to

· Develop culture methods and

 Optimize media formulations, growth and culturing conditions and scalability of production of MKP for preclinical efficacy, safety and

assays for the expansion,

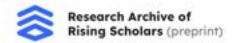
characterization and production of sufficient quantity MKP to initiate and complete IND enabling

related IND studies.

demonstrate effectiveness and improvement in therapeutic

specific to neuroprogenitor cells; 2. Whether the drug reduces radiotherapy-induced neuronal atrophy and cognitive impairment; and 3. How the drug affects neuroprogenitor cells and generation of new neurons.

• Perform preclinical studies to



amino acid peptide);

Biotherapeutics,

Galveston, TX

Fullerene-based

radioprotectors; Luna

Thrombocytopenia CLT009, human allogenic Fast track 2012 Ongoing

Innovations Inc.,

Roanoke, VA

megakaryocyte

progenitors

Phase I

Brain injury

Chrysalis

Indication	Drug; company	type	started	status	Model	Aims
Lung injury	BIO300 (synthetic genistein); Humanetics Corp., Minneapolis, MN	Fast track	2012	Ongoing	Mouse xenograft of NSCLC tumor model and NSCLC patients.	 Perform efficacy studies in mouse model to demonstrate inhibition of tumor growth and mitigation of radiation-induced lung damage. File IND for the use of BIO300 in patients receiving radiotherapy for NSCLC. Conduct phase II clinical study to assess safety and effect of BIO300 in improving the morbidity and mortality in patients receiving radiation therapy.
Brain injury	TP508 (biotherapeutic, 23 amino acid peptide); Chrysalis Biotherapeutics, Galveston, TX	Phase I	2011	Transitioned to phase II	Cell lines and mouse xenograft orthotopic model.	Optimize dose and schedule for vascular protection. Demonstrate protection to brain tissue from radiotherapy damage. Determine whether the protection is selective to normal tissue without altering radiation cell killing of cancer cells.
Brain injury	TP508 (biotherapeutic, 23	Phase II	2013	Ongoing	Mouse orthotopic	 Determine the following: 1.

xenograft model.

Cell lines and animals.

Ex vivo cell culture

expansion.

Continued.

2014 Ongoing

[&]quot; All information provided here and in the text is publicly accessible at http://projectreporter.nih.gov/reporter.cfm, except for funds distributed in 2015. While this information is accessible on the website, http://projectreporter.nih.gov/reporter.cfm, at the end of FY 2015, the company BioMimetix has kindly agreed to publicly release this information in this article.

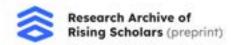


Table 2. Summary of activities in the Radioprotectors and Radiomitigators Portofolio. From Prasanna et al. (2015) [8].

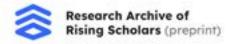
menopause, vaginal dryness, radiation-induced proctitis, bowel and bladder toxicity, and many others. Not only can those effects hinder a pregnant patient in their ability to sustain their pregnancy and deliver their offspring, but it would likely impact the fetus as well. Also, Table 3

(UP TO 2ND WEEK)	(SRD TO STH WEEK)	(6TH to ESTH WEEK)	POSTCONCEPTION (14TH TO 23RD WEEK)	POSTCONCEPTION (24th WEEK TO TERM)
	Noncano	or HEALTH EFFECTS NOT DETECT	TABLE	
Failure to implent may increase slightly, tail surviving embryos will probably have no significant (noncancer) health effects.	Growth restriction possible	Growth restriction possible	Noncancer health effects uni	hety
> 0.5 Gy (50 rads) be espectant mother may e especianing acute idiation syndrome in this ings, dispending on her hole-body dose. Faiture to impoint will thely be high, dispending on dose, but surviving embryos will probably how no significant (noncancer) health effects.		Probability of miscarriage may increase, depending on dose. Growth restriction is likely.	Phobability of miscarrage may ecrosse, depending on dose. Growth restriction is possible, depending on dose. (Less likely than during the 6th to 10th weeks, postconception). Phobability of major malformations may increase.	Mecamings and recreated death may occur, depending on dose, ⁴
y is possible during this period a finability (IG 0) is 40% after an</td <td>t doses > 0.5 Gy. exposure of 1 Gy from 8th to 15</td> <td></td> <td></td> <td></td>	t doses > 0.5 Gy. exposure of 1 Gy from 8th to 15			
guitin. The Indicated disser and times post or	months an approximations			
ents of absorbed done and refer the amount o looky total about. The enterprise abouthed dos	of energy deposited into a mass of focuse (10 or less), p. the document are positived to be	ty - 100 radio), in this document, the absorbed translants, gamens, or a calculum.	drove in West shows	
0.000	Failure to implient may increase slightly, but surviving embryon will probably have no significant (noncanorir) health effects. Failure to implient will likely be high, depending on dose, but surviving embryos will probably have no significant (noncanorir) health effects. It for intellectual disability in 6th y is possible during this period a linability (IQ	Failure to implant may increase slightly, but surviving embryos will probably have no significant (noncancer) health effects. Failure to implant will thely be high, depending on dose, but surviving embryos will probably have no significant (noncancer) health effects. Frailure to implant will thely be high, depending on dose, but surviving embryos will probably increase, depending on dose. *Probability of miscreasage may increase. *Probability of miscreasage may increase. *Probability of	Failure to implant may increase slightly, but surviving embryor will probably have no significant (noncancer) health effects. Failure to implant will tikely be high, depending on dose, but surviving embryos will probably an inverse depending on dose. -Probability of miscarrage may increase, depending on dose, but surviving embryos will probably now no significant (noncancer) health effects. -Probability of miscarrage may increase, depending on dose, health effects, increases, depending on dose, necessary, beath effects. -Probability of miscarrage may increase, depending on dose, necessary increases, depending on dose, necessary, beath effects. -Probability of miscarrage may increaseGrowth restriction is likely -Probability of miscarrage may increase, depending on dose, necessary in state of the second of dose increasesGrowth restriction is likely -Probability of miscarrage may increaseGrowth restriction possible of major may increase and increaseGrowth restriction possible of miscarrage may increaseGrowth restriction possible of miscarrage may increaseGrowth restriction possible of miscarrage may increaseProbability of miscarrage may increaseGrowth restriction possible of miscarrage may incre	Failure to implant may increase slightly, but surviving embryon will probably have no significant (noncancer) health effects. Failure to implant will likely be high, depending on dose, but surviving embryos will probably of miscarrage may increase, depending on dose, have no significant (noncancer) health effects. -Probability of miscarrage may increase, depending on dose, have no significant (noncancer) health effects. -Probability of miscarrage may increase, depending on dose, however, depending on doseProbability of miscarrage may increase, depending on dose, class likely than discincion in likely increase, depending on doseGrowth restriction in likely increaseGrowt

Table 3. Potential health effects (other than cancer) of prenatal radiation exposure. From CDC (2024) [3].

reveals that radiation doses between 0.10 Gy and 0.50 Gy can lead to the failure to implant and possible growth restriction depending on how many weeks pass post-conception. The effects are more severe for doses above 0.50 Gy. Such doses can result in side effects such as miscarriage, major malformations, and neonatal death.

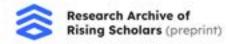
Also, some of the methods mentioned in Table 4 require large doses. Sometimes doses must be greater than 60 Gy to treat some cancers. That would require the patient to compromise between their health and the health of their offspring.



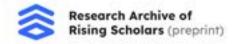
Common indica	ations for radiotherap	у.		
Cancer	Role of radiotherapy	Example of Indication	Comments	Outcomes
Breast	Adjust matrient	Early stage after wide local exchlors	In selected cases may be given intraoperatively (mature data awaited)**	Reduces fest recurrence at 10 years from 35.0% to 19.3% to 19.3% reduces 15 year absolute risk of death from breast cancer by 3.8% fluor 25.2% to 21.4% compared with no radiotherapy."
		High risk misstectomy patients		Reduces local recurrence at 5 years (From 2.7% to 6%) and reduces 15 year absolute risk of death from breast cancer by 5.4% (from 60.2% to 54.7%) compared with no radiative app*
				After breast radiotherapy the hagard ratio for death from heart disease is 1.27 and lung cancer 1.78 compared with no radiotherapy (overall mortality still reduced) ²⁹
Prostate	Primary Insutment	Early stage	Radiotherapy alone (brachytherapy in some cases) as a treatment option rather than surveillance or surgery	Smilar outcomes to surgery ²⁰ , 93% provide specific arrigen corosil with brachytherapy at 7 years in low risk disease ²⁰ .
		Locally advanced	EBRI is often used in combination with androgen deprivation therapy	74.1% and 71 A% prostes specific antigen control and overall survival, respectively, at 10 years for imperable surrours."
ling	Primary treatment	Locally advenced tumours or comorbidity	Optimal outcomes using CHART or chemoradiation, radical high dose treatment for small tumours.	Concurrent chemicadiation improves 2 year survival by E% compared with radiotherapy atone", OHATI improves 2 year survival from 20% to 29% compared with conventional radiotherapy."
	Stereotacticablative radiotherapy	Medically insperable fumours		Meture sufcome data awaited
Head and neck	Primary and adjuvent treatment	Can be used in most cancers to aid organ preservation	Often given with displatin	Syear survival: 80-90% in stage 1-2 tumours, 60-70% in stage 3-4 tumours ⁴⁶
Recture	Neoassuvant tramment	To downstage bulky tumours at risk of involved resection margins	Given as shortcourse (5 days) or long course (5 weeks) treatment	Cochrane review shows improved overall survival (by 2%) and local recurrence lates Pieterogeneous across histis compared with no radiotherapy***
Systemological	Prinary and adjusted Insulment	Cervializace	Primary chemoradiotherapy is standard of care in all but evrly stage I cervical cancers.	
		Endonetrial cancer		Adjuvant EBIT reduces locoregional recurrence from 8.5% to 2.5% compared with surgery allone but has no effect on survival.
Brain	Primary and adjovent.	After debuilding surpery	Concurrent temporalization improves survival.	At doses above 60 by intproves median survival from 18 to 42 weeks compared with supply atmoral.

Table 4. Common indications for radiotherapy. From Ahmad et al. (2012)[1].

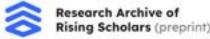
Radiotherapy can be fatal for both the patient and their offspring if not managed safely. It is necessary to find a solution for administering radiotherapy safely and effectively. Although Table 3 lists the consequences of patients receiving different dosages, the effects of a dose greater than 0.50 Gy are probably insignificant among surviving embryos if administered after two weeks post-conception. Health effects are unlikely for doses between 0.10 Gy and 0.50 Gy. Doses under 0.10 Gy have not posed any harmful effects. Keeping the dosage amount low when possible will help ensure the safety of patients and their offspring. Table 2 summarizes various tests conducted on animal models and samples to improve the safety of radiotherapy and reduce its side effects. A few models were used to test certain drugs and determine their safety and effectiveness. The methods mentioned in the study from the article serve as potential ways to improve radiotherapy safety and provide solutions to already existing side effects.



	Purpose of study	Research findings
Article (year)	- To analyse different roles of radiotherapy	-For <i>breast cancer</i> , adjuvant treatment is used
[1] (2012)	depending on the type of cancer being treated	-Examples of indication are early state wide local excisions and high risk mastectomy patients
	- Records outcomes of the each treatment depending on the	-Reduces (for early stage) first recurrence at 10 years (from 35.0% ro 19.3%), reduces 15 year absolute risk of death by 3.8% (from 25.2% ro 21.4%) compared to no radiotherapy
	indications for each cancer	-Reduces (for high risk mastectomy) local recurrence at 5 years (from 23% to 6%) and reduces 15 year absolute risk of death by 5.4% (from 60.1% ro 54.7%) compared with no radiotherapy
		-After treatment, the hazard ratio for death from heart disease is 1.27 and lung cancer 1.78 compared with no radiotherapy
		-For <i>prostate cancer</i> , primary treatment is used, and identification is early stage and locally advanced
		-It is used alone rather than with surveillance or surgery
		-Similar outcomes with surgery
		-93% prostate specific antigen control with brachytherapy at 7 years low risk disease
		-ERBT is often used in combination with androgen deprivation therapy and results in 74.1% and 71.4% prostate specific antigen control and overall survival, respectively, at 10 years in inoperable tumors
		-For <i>lung cancer</i> , primary treatment (specially, CHART or chemoradiation) is used, and indication is locally advanced tumors or comorbidity
		-Stereotactic ablative radiotherapy is also used, and indication is medically inoperable tumors
		-Need to use a high dose for optimal outcomes when using CHART
		-CHART improves 2 year survival rate by 8% compared with radiotherapy alone (from 20% to 29% compared with conventional radiotherapy)
		-No data recorded on the outcome of stereotactic ablative radiotherapy
		-For head and neck cancer, primary and adjuvant treatment is used, and it can be used in most cancers to aid organ preservation (often given with cisplatin)
		-5 year survival (80-90% in stage 1-2 tumors, and 60-70% in stage 3-4 tumors)
		-For <i>rectum cancer</i> , neoadjuvant treatment is used to downstage bulky tumors at risk of involved resection margins (given as short course of 5 days or long course of 5 weeks treatment)
		-Improved overall survival by 2% and local recurrence rates compared with no radiotherapy



		-For gynecological cancer (cervical and endometrial), primary and adjuvant treatment are used
		-In cervical cancer, primary treatment is used in all stages except for early stage
		-In cervical cancer, concurrent cisplatin and radiotherapy improves 5 year survival from 60% to 66%
		-In endometrial cancer, adjuvant ERBT reduces locoregional recurrence (from 8.5% to 2.5%) compared with surgery alone but has no effect on survival
		- For <i>brain cancer</i> , primary and adjuvant treatment is used after debulking surgery
		Concurrent temozolomide improves survival
		-Doses above 60 Gy improves median survival from 18 to 42 weeks compared with surgery alone
[3] (2024)	-Summarizes the potential risks from	-Less than 0.10 Gy have not shown any effects
[3] (2024)	radiotherapy (not cancer related)	-0.10-0.50 Gy may increase failure to implant after two weeks post conception (unlikely the effects will be significant)
	-Intended to help physicians advise pregnant women who	-Growth restriction possible for 3rd to 13th weeks post conception
	may have been exposed to radiation	-Health effects unlikely for 14th week post conception to term
	-Not a definitive recommendation	-Dosage greater than 0.50 Gy can make the failure to implant high after two weeks post conception (probably not significant among surviving embryos)
	-Data is approximate	-Probability of misscarriage, major malformations, and growth restriction may increase after 3rd to 13th week post conception
		-Same effects as 3rd to 13th week post conception except the likelihood is lower (14th to 23rd weeks)
		-Miscarriage and neonatal death may occur 24th week to term

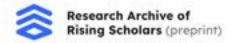


>	Rising	Scholars	(preprint)

(2015)

- -Summarizes the activities of radioprotectors and radio mitigators
- -Looks at tested animals and describes the tests done on them
- -Models used to test ways to mitigate radiation effects

- -The mouse model of pelvis irradiation is used for enteritis (indication)
- -The aims are to evaluate radio protecting/radio mitigating effect on gastrointestinal injury and to evaluate the effect on cancer radiosensitivity
- -The mouse model of gastrointestinal acute radiation syndrome is used for enteritis (indication)
- -The aims are to perform proof of concept studies to show that a particular drug will reduce GI-ARS following abdominal or pelvic radiation
- -The rat for acute radiation induced proctitis is used for proctitis (indication)
- -Aims to demonstrate efficacy in mitigation of radiation induced proctitis and to develop plans to demonstrate that PAAG does not protect cancer cells during radiotherapy
- -The mouse model of head and neck cancer is used for mucositis (indication)
- -Aims to demonstrate protective effect to skin and oral mucosa after single and fractionated multiple radiation dose regimens and demonstrate safety and efficacy of a specific drug in combination with radiotherapy
- -The hamster cheek is used for mucositis (indication)
- -Aims to develop RLIP as a topical mouthwash and to test efficacy, systemic absorption, and demonstrate no tumor protection
- -The mouse model and patients with head and neck cancer is used for mucositis (indication)
- -Aims to perform dose and schedule optimization studies for protection from radiation induced oral mucositis, identify and qualify a GMO manufacturing site, submit an IND application for JVRSOD, and perform phase I safety and phase II efficacy clinical trials
- -The mouse model of head and neck squamous cell carcinoma is used for mucositis (indication)
- -Aims to establish optimum dose schedule to reduce xerostomia and mucositis and to demonstrate that a particular drug does not interfere with standard of care
- -The cell lines and mouse model of lung injury is used for lung injury (indication)
- -Aims to examine whether a drug reduces tumor cell killing in vitro, demonstrate efficacy in reducing radiation-induced lung injury in vivo, and demonstrate that the drug does not affect tumor cell killing induced by radiation in vivo
- -The mouse xenograft of NSCLC tumor model and NSCLC patients is used for lung injury (indication)
- -The cell lines and mouse xenograft orthotopic model is used for brain injury (indication)
- -Aims to optimize dose and schedule for vascular protection, demonstrate protection to brain tissue from radiotherapy damage, and determine whether the protection is selective to normal tissue without altering radiation cell killing cancer cells

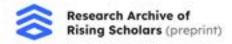


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		-The mouse orthotopic xenograft model is used for brain injury (indication)
		-Aims to determine whether a particular drug protects also cancer stem cells or whether its protective effects are specific to neural progenitor cells, whether the drug reduces radiotherapy-induced neuronal atrophy and cognitive impairment, and how the drug affects neural progenitor cells and generation of new neurons
		-The cell lines and animals are used for brain injury (indication)
		-Aims to perform preclinical studies to demonstrate safety and effectiveness and improvement in therapeutic ratio
		-Ex vivo cell culture expansion is used for thrombocytopenia (indication)
		-Aims to develop culture methods and assays for the explanation, characterization and production of sufficient quantity MKP to initiate and complete IND enabling studies and to optimize media formulations, growth and culturing conditions and scalability of production for MKP for preclinical efficacy, safety and related IND studies
	-Summarizes	- External beam radiotherapy (EBRT) is to delivered from a distance
[14](2020)	radiotherapy interventions in the management of cervical cancer	-The intents/advantages are that is is curative for small to large lesions in combination with BT and chemotherapy, and that it is palliative to control bleeding and/or pain
	-Describes the procedures, intents/advantages, and risks of each type	-The risks are infertility, menopause, vaginal dryness, bowel, urinary, hematological and skin toxicity
	of radiotherapy listed in the chart	-Brachytherapy (BT) is delivered from a sealed radioactive source placed inside the vagina and uterus, close to the tumor
		-The intent/advantage is that it is curative for small to large lesions in combination with ERBT
		-Risks are vaginal stenosis, vaginal dryness, radiation proctitis, bowel and bladder toxicity, and that it may require anesthesia
		-After adjuvant radiotherapy (aRT) is administered, EBRT and/or BT are administered after surgery
		-The intent/advantage is that it eradicates any microscopic disease in the irradiated area
		-The risks are bowel, urinary, hematological, and skin toxicity

Table 5. Summary of research findings.

Discussion

The findings reveal that radiotherapy is necessary to treat cancer, can cause serious side effects if patients and their offspring are not safely protected, and that various ways to remedy the effects of treatment exist. Such information can be taken into consideration when deciding the



best course of action when a pregnant patient needs to receive treatment for cancer. Although the meta-analysis reveals information for combating the issues with radiotherapy, the study has some limitations. The articles used for primary research are not very recent. The oldest article was published in 2012. Also, the data from Table 3 is approximate and not intended to serve as a definite recommendation. In addition, Table 2 does not include the results of the recorded methods. The primary data collection was limited to older data because no resources were available for conducting an experiment and acquiring new observations. However, anyone wishing to conduct further research into the issue of radiotherapy safety could build off the meta-analysis by conducting experiments and recording more exact data. Furthermore, they can replicate the tested methods in Table 4 to analyze the outcomes.

Conclusion

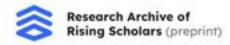
Radiotherapy has many dangerous implications, especially for fetuses. However, it does not have to stay that way. Radiotherapy can be improved by implementing certain devices or treatments during procedures, incorporating aspects of other cancer treatments into radiotherapy, following strict treatment regulations, and individualizing treatment plans for pregnant patients. By doing these things, fetuses exposed to the treatment will not have to suffer the lifelong effects of radiotherapy. Mothers will be able to receive radiotherapy without having to compromise the health of their future son or daughter.

References

- [1].Ahmad, S. S., Duke, S., Jena, R., Williams, M. V., & Burnet, N. G. (2012). Advances in radiotherapy. *BMJ: British Medical Journal*, *345*(7886), 33–38. http://www.jstor.org/stable/41724503
- [2].Butson, Macinley. (2017). How ancient technology inspired my award-winning inventions [Video]. *Ted*. https://www.ted.com/talks/macinley butson how ancient technology inspired my award winni

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- [3].CDC (2024). Brochure for Physicians: Prenatal Radiation Exposure. https://www.cdc.gov/radiation-emergencies/media/pdfs/2024/09/19_311498-A_Douglas_Update s Prenatal RadiationExposure 508c 2.pdf
- [4].Chuba, P. J., Aronin, P., Bhambhani, K., Elchenhorn, M., Zamarano, L., Clanci, P., Muhlbauer, M., Porter, A. T., & Fontanesi, J. (1997). Hyperbaric oxygen therapy for radiation-induced brain injury in children. *Cancer*, 80(10) 1883-2023. https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/%28SICI%291097-0142%2819971115 %2980%3A10%3C2005%3A%3AAID-CNCR19%3E3.0.CO%3B2-0



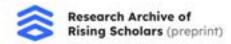
- [5].Doyle, Bill. (2012). Treating cancer with electric fields [Video]. Ted. https://www.ted.com/talks/bill_doyle_treating_cancer_with_electric_fields
- [6].IAEA (2000).Pregnant women in radiotherapy. In *Annals of the ICRP Publication 84 Pregnancy and Medical Radiation*. J Valentin (ed.) Pergamon Press. https://www.iaea.org/resources/rpop/health-professionals/radiotherapy/pregnant-women
- [7].Lakhwani, O. P., Dalal, V., Jindal, M., & Nagala, A. (2019). Radiation protection and standardization. *J. of Clinical Orthopaedics and Trauma*, 10(4) 738-743.

https://www.sciencedirect.com/science/article/abs/pii/S097656621830167X

- [8].Prasanna, P. G. S., Narayanan, D., Hallett, K., Bernhard, E. J., Ahmed, M. M., Evans, G., Vikram, B., Weingarten, M., & Coleman, C. N. (2015). Radioprotectors and Radiomitigators for Improving Radiation Therapy: The Small Business Innovation Research (SBIR) Gateway for Accelerating Clinical Translation. *Radiation Research*, *184*(3) 235–248. http://www.jstor.org/stable/24546020
- [9].Ramenghi, L. A., Ricci, D., Mercuri, E., Groppo, M., De Carli, A., Ometto, A., Fumagalli, M., Bassi, L., Pisoni, S., Cioni, G., & Mosca, F. (2010). Visual performance and brain structures in the developing brain of pre-term infants. *Early Human Development*, 86(1) 73-75. https://www.sciencedirect.com/science/article/abs/pii/S0378378210000125
- [10].Ring, A. E., Smith, I. E., & Ellis, P. A. (2005). Breast Cancer and Pregnancy. *Annals of Oncology* 16(2) 1855-1860. https://www.sciencedirect.com/science/article/pii/S0923753419477922
- [11]. Schwab, R., Anic, K., & Hasenburg, A. (2021). Cancer and Pregnancy: A Comprehensive Review. *Cancers* 13(12) 3048.

https://www.mdpi.com/2072-6694/13/12/3048

- [12]. Sergieva, K., Kostova, P., & Zlatkov, V. (2017). Trends in radiation protection of patients in modern radiotherapy. *Doklad IAEA Radiation Protection Conference. Researchgate.net* https://www.researchgate.net/profile/Katia-Sergieva/publication/322064907_Trends_in_radiation_protection_of_patients_in_modern_radiotherapy/links/5fa3f31792851cc286960834/Trends-in-radiation-protection-of-patients-in-modern-radiotherapy.pdf
- [13]. Soria, B., Martin-Montalvo, A., Agueilera, Y., Mellado-Damas, N., Lopez-Beas, J., Herrera-Herrara, I., López, E., Barcia, J. A., Alvarez-Dolado, M., Hmadcha, A., & Capilla-Gonzáles, V. (2019). Human Mesenchymal Stem Cells Prevent Neurological Complications of Radiotherapy. *Front. Cell. Neurosci.*, 13 article 204. https://www.frontiersin.org/articles/10.3389/fncel.2019.00204/full



[14]. World Health Organization. (2020). Core elements of cervical cancer management. In WHO Framework for strengthening and scaling-up services for the management of invasive cervical cancer (pp. 15–44). *World Health Organization*.

http://www.jstor.org/stable/resrep30127.9