"Improved Treatment for Cervical Cancer – Concurrent Chemotherapy and Radiotherapy" (1999), by Gillian Thomas [1]

By: Darby, Alexis Keywords: Cervical Cancer [2] chemotherapy [3] Radiation [4] cancer treatment [5] HPV [6] Papillomavirus [7] Clinical trial [8]

On 15 April 1999, physician Gillian Thomas published the editorial "Improved Treatment for Cervical Cancer – Concurrent Chemotherapy and Radiotherapy," henceforth "Improved Treatment," in *The New England Journal of Medicine*. In that editorial, she discusses the potential benefits of combining chemotherapy drugs with radiation [9] to treat women with cervical cancer. At the time, healthcare professionals rarely treated cervical cancer by combining chemotherapy or radiation [9]. Two months prior to Thomas's publication, the US National Cancer Institute [10], headquartered in Bethesda, Maryland, released an announcement advocating for combining chemotherapy with radiation [9] based on clinical trial results. In "Improved Treatment," Thomas summarized the results of those clinical trials that had led to the announcement and communicated a new way to treat invasive cervical cancers, which persists as of 2019.

In "Improved Treatment," Thomas discusses concepts related to cervical cancer. Cervical cancer is a cancer located in a woman's cervix [11], or the narrow tube that connects thevagina [12] and uterus [13]. Cervical cancer starts with non-cancerous cellular changes and can progress into advanced, cancerous growths. In the 1980s, scientists discovered that a sexually-transmitted virus called human papillomavirus, or HPV, caused most cases of cervical cancer. As of 2019, there are screening and early detection programs for both HPV and cervical cancer. There is also a vaccination that people can receive to prevent them from contracting the virus, and therefore, that can prevent cervical cancer in women.

Thomas also discusses concepts related toradiation [9] techniques, chemotherapy drugs, and clinical trials in "Improved Treatment." Radiation therapy involves the use of x-rays, a type of high-energy electromagnetic radiation [9], or other sources to kill cancer cells. A machine outside of the human body can emit the x-ray [14] therapy. Healthcare professionals can also place radioactive material inside the body. Chemotherapy is the use of drugs designed to stop the growth of cancer cells, and physicians administer them to patients by mouth, injection, or infusion. Thomas documents different types of chemotherapy drugs which were previously successful in animal studies and would move on to human trials. In the article, Thomas discusses the two forms of treatment in terms of clinical trial results. Phase I and II trials involve testing drugs on healthy volunteers to determine their safety and efficacy in healthy populations. Phase III trials involve testing drugs on sick populations to determine their effectiveness. In "Improved Treatment," Thomas analyzes the Phase III clinical trials' results about combining radiation [9] and chemotherapy for women with cervical cancer.

When "Improved Treatment" was published, Thomas worked as aradiation [9] oncologist at the University of Toronto in Toronto, Canada. Thomas received both her bachelor's degree in science and medical degree at the University of Toronto. According to the University of Toronto, as of 2019, Thomas is an emeritus professor of radiation [9] oncology.

Thomas organizes the editorial into three major sections. In the first section, Thomas briefly discusses the history of cervical cancer treatment in the United States and how physicians reached the conclusion to combine chemotherapy drugs with radiation [9] to treat cervical cancer. In the second part, she details three particular studies which had recently published their Phase III clinical trial results. *The New England Journal of Medicine*published the results of those clinical trials in the same issue as Thomas's article. Finally, in the third section, Thomas makes recommendations for future improvements in cervical cancer treatment.

In the first section of "Improved Treatment," Thomas analyzes past treatment methods for cervical cancer. Thomas asserts that there had been no significant improvements to the treatment of cervical cancer since the invention of radiation [9] therapy in the 1950s. Despite screening programs for cervical cancer, Thomas writes that, in the United States alone, there were still over 14,000 new cases of invasive, advanced cervical cancer annually as of the editorial's 1999 publication date. In economically developing countries, the prevalence of cervical cancer and the rates at which healthcare professionals can diagnose terminal disease are higher, and cervical cancer is the leading cause of cancer deaths for women. Thomas adds that external pelvic radiation [9] had been the leading treatment for advanced disease. With pelvic radiation [9], physicians can either directly apply x-rays into a woman's vagina [12] or, more commonly, physicians can apply externalradiation [9] with machines called linear accelerators. With the external treatment, physicians found that the overall five-year survival rates for women was around sixty-five percent, ranging from fifteen to eighty percent depending on the progression of the disease. The author adds that although increasing the dose of pelvic radiation [9] could potentially improve the control of cervical cancer, physicians had to limit the

radiation [9] due to potentially disfiguring and fatal side effects, such as burns and tissue death in and around the uterus [13].

Thomas then discusses the potential benefits physicians and scientists predicted for the administration of radiation [9] and chemotherapy drugs at the same time, in comparison to the use of radiation [9] alone. According to Thomas, scientists theorized that they could use radiation [9] and chemotherapy simultaneously without having to extend either treatment. Using the treatments simultaneously could potentially increase the amount of tumor cells killed in a given time frame. With radiation [9], physicians use x-rays to damage the area of the body with cancer to destroy the cancer cells and surrounding tissues to prevent new growth. Preventing new growth prevents cancer from spreading through the body.

Thomas states that, theoretically, chemotherapy could stop the body from repairing damage from radiation [9] since chemotherapy reduces the growth of rapidly-growing cells. Cells of the immune system are rapidly-growing, especially when responding to a bodily injury such as radiation [9]. If the immune cells cannot repair damage from radiation [9] due to chemotherapy usage, then that could reduce the efficacy of the radiation [9] treatment. That means that the radiation [9] alone could be more effective at stopping the growth and spread of cancer cells. However, Thomas also states that physicians would administer less chemotherapy when combined with radiation [9] than that given with chemotherapy alone in order to prevent side effects from the combination therapy.

According to Thomas, such a combination would not affect existing cancer metastases, or the development of secondary cancer growths away from the origin of the cancer, since the chemotherapy would not be as strong and because radiation [9] typically targets only one area of the body. According to a 2006 article from the scientific journal *American Family Physician*, when cancer metastases to the liver and lungs it limits life expectancy to around six months and when cancer metastases to the lymph nodes it limits life expectancy to around six weeks. Thomas concedes that a combination therapy may not be as beneficial as some physicians originally thought but goes on to provide trial results, which investigated the combination therapy further.

As Thomas moves into her discussion on the successful Phase III trials, she first discusses the Phase I and II trials which established that treatment involving chemotherapy and radiation [9] could be safely combined. Physicians studied three chemotherapy drugs with healthy populations during the Phase I and II trials, including cisplatin, fluorouracil, and mitomycin, which are drugs that kill cells. Thomas notes that since radiation [9] alone is fairly effective at killing cancer cells, the researchers could only determine what benefits, if any, a combined chemotherapy and radiation [9] regimen offered to patients by studying a sick population, as opposed to the healthy populations in Phase I and II trials. She notes that three studies involving Phase III clinical trials answered the questions physicians had on whether a combined regimen of chemotherapy and radiation [9] would benefit women with cervical cancer.

Thomas describes one of the first Phase III trials conducted by Henry M. Keys and colleagues, which compared two groups of women who received either radiation [9] alone or a six-week combination of radiation [9] in conjunction with the chemotherapy drug, cisplatin. The women in the study had early-stage cervical cancer. According to Thomas, women who received the combined regimen tolerated it well and it did not increase the median treatment time, which was fifty days for both test groups. That means that the combination regimen worked about as well as the radiation [9] alone on average for the women in the study. However, for stage IB cervical cancer, which is a less-aggressive form of cervical cancer, Thomas asserts that the particular combination of radiation [9] and chemotherapy worked better than radiation [9] alone, resulting in better control of cervical cancer, a reduction [15] in metastases, and prolonged patient survival.

Thomas then describes the results of the therapeutic combination for women with more advanced cervical cancer as studied in another Phase III trial conducted by Peter Rose and colleagues. The authors assessed over 500 women with late-stage cervical cancers who were randomly assigned to receive one of three different courses of chemotherapy in combination with radiation [9]. Each experimental group received the same levels of radiation [9], but different types and amounts of chemotherapy. Almost half of the women in the study had advanced cervical cancer that had either metastasized to the bladder or the pelvic wall. The survival rates were higher in the group of women who received the same drug used by Keys and colleagues, cisplatin. Thomas states that cisplatin could become the favorable option for chemotherapy due to decreased risks of side effects and more favorable long-term survival rates. Among the Keys and colleagues and Rose and colleagues experiments, Thomas states that the cisplatin-based chemotherapy in addition to radiation [9] therapy was undoubtedly beneficial.

In the third paper that Thomas discusses, by Mitchell Morris and colleagues, scientists studied almost 400 women with a range of cervical cancer progression. The experimental groups received either a combination of cisplatin and fluorouracil chemotherapy drugs with only pelvic radiation [9], or radiation [9] alone aimed at both the pelvis and pelvic lymph nodes rather than just the pelvis. Rose and colleagues found that the chemotherapy and radiation [9] group had higher survival rates at seventy-three percent as compared with a fifty-eight percent survival rate for women who received radiation [9] alone. Thomas mentions that it is difficult to determine whether those results apply to all stages of cervical cancer since the women who would potentially receive the most benefit of the single-radiation [9] group would be those with advanced cancers. That is because that therapy applied radiation [9] to the lymph nodes, and women with cervical cancer typically only have lymph node involvement when the cancer has progressed to become more advanced. Furthermore, only thirty percent of the women in the study had advanced cervical cancer that had spread to their lymph nodes.

In “Improved Treatment,” Thomas also discusses the impact of those three studies on the national discourse about cervical

cancer treatment at the time. Thomas makes a call to action at the end of her article by claiming that more research is needed before physicians can definitively state which drugs or regimens are optimal in treating cervical cancer. However, Thomas also argues that it is reasonable to assert that cisplatin and radiation [9] therapy together may result in better survival outcomes for women with cervical cancer. She made those claims based on the results of the three major studies she included in her editorial, as well as using the US National Cancer Institute's clinical announcement that physicians should make strong consideration in adding chemotherapy drugs to radiation [9] in treating cervical cancer as further evidence. Thomas concludes the article by stating that those studies are an important step toward making cervical cancer easier to treat.

Thomas's 1999 publication "Improved Treatment," called physicians to prioritize treating women who had cervical cancer with combination regimens of chemotherapy and radiations. According to a 2007 study in the journal *International Journal of Radiation Oncology Biology Physics*, women who received cisplatin, a kind of chemotherapy drug, and radiation [9] treatments together saw survival rates up to eighty percent in the two years following treatment.

Sources

1. Beriwal, Sushil, Gregory N. Gan, Dwight E. Heron, Raj N. Selvaraj, Hayeon Kim, Ron Lalonde, Joseph L. Kelley, and Robert P. Edwards. "Early clinical outcome with concurrent chemotherapy and extended-field, intensity-modulated radiotherapy for cervical cancer." *International Journal of Radiation Oncology Biology Physics* 68 (2007): 166–71.
2. Finn, John W. "Determining prognoses for patients with terminal illnesses." *American Family Physician* 73 (2006): 2062–7.
3. Keys, Henry M., Brian N. Bundy, Frederick B. Stehman, Laila I. Muderspach, Weldon E. Chafe, Charles L. Suggs, Joan L. Walker, and Deborah Gersell. "Cisplatin, radiation [9], and adjuvant hysterectomy [16] compared with radiation [9] and adjuvant hysterectomy [16] for bulky stage IB cervical carcinoma." *The New England Journal of Medicine* 340 (1999): 1154–61. https://www.nejm.org/doi/pdf/10.1056/NEJM199904153401503?articleTools=true [17] (Accessed September 13, 2019).
4. Morris, Mitchell, Patricia J. Eifel, Jiandong Lu, Perry W. Grigsby, Charles Levenback, Randy E. Stevens, Marvin Rotman, David M. Gershenson, and David G. Mutch. "Pelvic radiation [9] with concurrent chemotherapy compared with pelvic and para-aortic radiation [9] for high-risk cervical cancer." *The New England Journal of Medicine* 340 (1999): 1137–43. https://www.nejm.org/doi/pdf/10.1056/NEJM199904153401501?articleTools=true [18] (Accessed September 13, 2019).
5. Rose, Peter G., Brian N. Bundy, Edwin B. Watkins, J. Tate Thigpen, Gunther Deppe, Mitchell A. Maiman, Daniel L. Clarke-Pearson, and Sam Insalaco. "Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer." *The New England Journal of Medicine* 340 (1999): 1144–53. https://www.nejm.org/doi/pdf/10.1056/NEJM199904153401502?articleTools=true [19] (Accessed September 13, 2019).
6. Thomas, Gillian M. "Improved treatment for cervical cancer—concurrent chemotherapy and radiotherapy." *The New England Journal of Medicine* 340 (1999): 1198–200.

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