

## 18 YEARS OF CONFORMATION RADIOTHERAPY AT NAGOYA UNIVERSITY HOSPITAL

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### ABSTRACT

Conformation radiotherapy is one of the best techniques for minimizing the radiation dose absorbed by the surrounding normal tissue while delivering a high dose to a cancerous target area. The cases of all patients who underwent external irradiation at Nagoya University Hospital from 1975 to 1992 were reviewed. A total of 5740 patients with 6179 lesions were irradiated during this time, and 3795 treatment plans involved radical intended irradiation. Of the 5740 patients, 1017 had head and neck cancer, 982 had cervical cancer, 506 had lung cancer, 439 had primary brain tumors, 308 had esophageal cancer, 1213 had metastatic tumors, and 1275 had other types of tumors. The total number of treatment plans per year decreased from 442 in 1975 to 292 in 1992. Likewise, the percentage of conformation radiotherapy performed in all patients decreased from 29.4% (130/442) in 1975 to 8.6% (25/292) in 1992. It occupied 14.5% (982/6179) of all intended plans, and 20% (775/3795) of radical treatment plans. The conformation technique was used in cases of cervical cancer (72%), esophageal cancer (65%) and primary brain tumors (25%). Boost Conformation radiotherapy represented 2% of all treatment planning and 29% of the conformation radiotherapy. Boost Conformation radiotherapy has recently become more popular and now represents more than 50% of conformation radiotherapy. With respect to cases of cervical cancer, the rates of local recurrence and late complications in cases treated by conformation radiotherapy were lower than in cases treated by two parallel opposed radiotherapy.

Key Words: Conformation radiotherapy, Hollow-out, Cervical cancer, Complications, Local control

### INTRODUCTION

Conformation radiotherapy, so named by Prof. Takahashi in 1961,<sup>1)</sup> has been developed in the Department of Radiology, Nagoya University School of Medicine.<sup>2-10)</sup> "Conformation" refers to making the shape of something (in this case the radiation field) conform to that of another (the target volume). Conformation radiotherapy essentially involves rotation therapy.<sup>1)</sup> Conformation radiotherapy is one of the best techniques for minimizing injury to the surrounding normal tissues while delivering a high radiation dose to the target area. There are essentially 2 methods or ideas involved in conformation radiotherapy which are applied to its clinical use. The first is primary irradiation from the beginning (Primary Conformation), and the second is adjuvant boost irradiation (Boost Conformation). The Primary Conformation technique, however, has a theoretical disadvantage in that it may increase volume-dose (absorbed dose by volume). The second method, Boost Conformation, was developed to address this problem and as such represents a modification of Primary Conformation. To date, there have been no reports on the historical review of conformation radiotherapy and its merits and limits. In this paper, we discuss the relative merits and demerits of conformation radiotherapy in the treatment of

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cervical cancer based on a review of all treatment plans undertaken at our hospital between 1975 and 1992.

## MATERIALS AND METHODS

We researched all the patients who underwent external irradiation at our institution from 1975 to 1992, and then divided them into the following 7 case groups: head and neck cancer, cervical cancer, lung cancer, primary brain tumor, esophageal cancer, metastatic tumor and others. In each group, conformation radiotherapy planning was counted and calculated as a percentage.

Conformation radiotherapy was most actively applied to cervical cancer at our institution. Cervical cancer was chosen as representative for evaluating conformation radiotherapy, based on the criteria of whether and to what extent the rate of local control and side effects improved. The rates of local recurrence and radiation damage to the rectum and bladder (local late complications) were compared between conformation radiotherapy (Conform), conform hollow-out conformation radiotherapy (H-Conform) and two parallel opposed radiotherapy (Bi-Portal) in radical intended patients from 1975 to 1992.

## RESULTS

A total of 6179 lesions in 5740 patients were irradiated at our institution from 1975 to 1992. Radical treatment irradiation was planned in 3795 patients. A total of 5740 patients were divided into the following 7 case groups: 1017 with head and neck cancer, 982 with cervical cancer, 506 with lung cancer, 439 with primary brain tumors, 308 with esophageal cancer, 1213 with metastatic tumors, and 1275 with other types of tumors. The total number of treatment plans per year decreased from 442 in 1975 to 292 in 1992. The percentage of conformation radiotherapy in all patients decreased from 29.4% (130/442) in 1975 to 8.6% (25/292) in 1992 (Fig. 1). It represented 14.5% (982/6179) of total patients, and 20% (775/3795) of

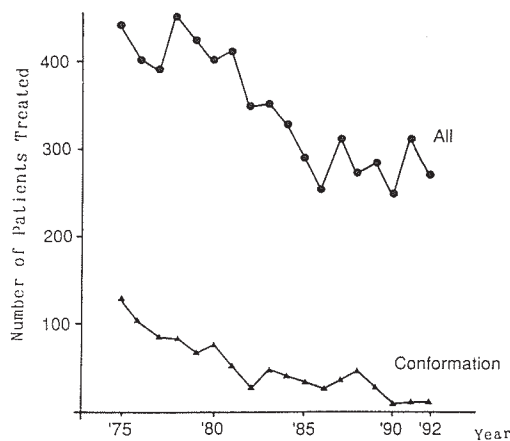


Fig. 1. The graph depicts the changes in the number of patients from 1975 to 1992. The "All" shows the total number of patients who underwent radiotherapy. The "Conformation" line shows the number of patients who were treated by Conformation Radiotherapy.

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radical patients. The number of cases of cervical cancer decreased from 85 in 1975 to 30 in 1991, but the number of patients with head and neck cancer, esophageal cancer, and brain tumors remained unchanged. The number of patients with metastasis for palliative treatment increased from 55 in 1975 to 87 in 1992 (Figs. 2 and 3). Conform was used for radical treatment in 72% (398/552) of cervical cancer cases, 65% (247/308) of esophageal cancer cases, and 25% (109/439) of primary brain tumor cases. Boost Conformation radiotherapy represented 2% of all treatment plans and 29% of Conform. Boost Conformation radiotherapy has become more popular, and now represents more than 50% of all Conform (Fig. 4).

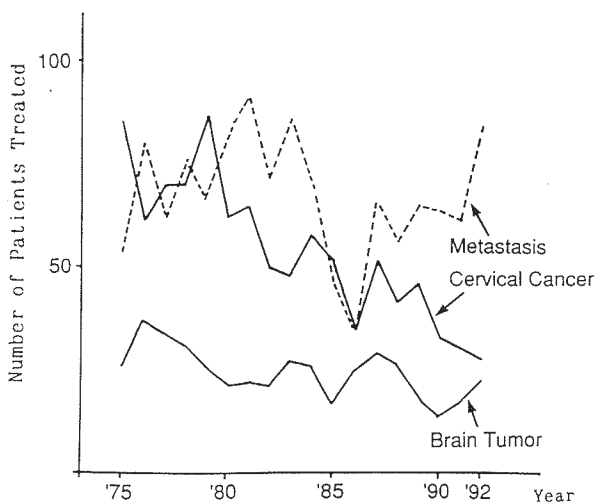


Fig. 2. The graph depicts the changes in the number of patients treated by radiotherapy for uterine cervical cancer, primary brain tumors, and metastatic tumors from 1975 to 1992.

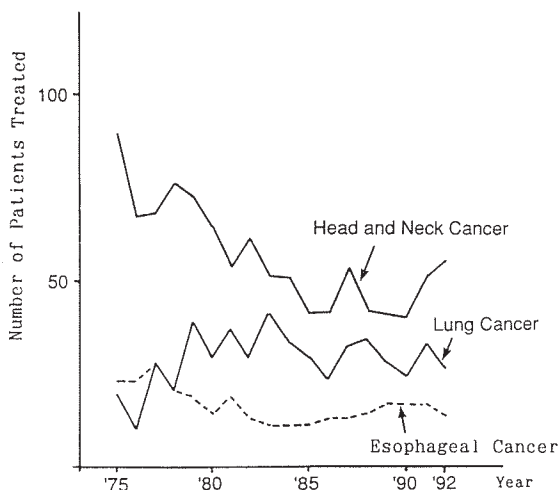


Fig. 3. The graph depicts the changes in the number of patients treated by radiotherapy for head and neck cancer, lung cancer and esophageal cancer from 1975 to 1992.

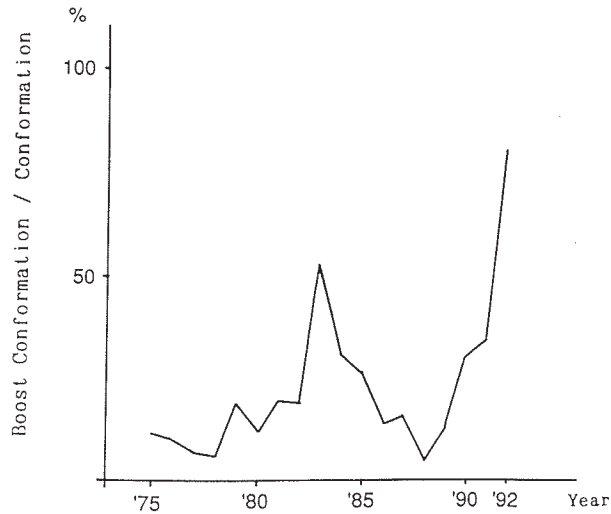


Fig. 4. The graph depicts the ratio of all patients treated with conformation radiotherapy to the number of patients treated with Boost Conformation radiotherapy from 1975 to 1992.

From 1975 to 1984, the dose of external irradiation applied to the whole pelvis to treat cervical cancer varied from 40 to 50 Gy. From 1975 to 1982, patients were treated by means of Bi-Portal or Conform irradiation. From 1982 to 1990, H-Conform irradiation was used. In 1985, the applied dose was increased from 40 Gy to 60 Gy by means of H-Conform irradiation. In Bi-Portal irradiation, the dose applied to the whole pelvis was 40 Gy, and some patients were treated with 15 Gy of center-block boost irradiation after 1985. For the treatment of cervical cancer, in 1985 we shifted our clinical application from intracavitary irradiation with low dose rate (LDR) to intracavitary irradiation with high dose rate (HDR). The dose of LDR was about 24 Gy at A point using  $^{226}\text{Ra}$ , with a dose rate of 0.5 Gy per hour. The dose of HDR was from 20 Gy to 16 Gy by four fractions at A point using  $^{60}\text{Co}$ , with a dose rate of 0.5 Gy to 0.3 Gy per minute. The rate of local control failure in Conform radiotherapy was 11/279 (3.9%) with LDR. In H-Conform radiotherapy, the source rate was 2/43 (4.6%) with LDR and 2/76 (2.6%) with HDR. In Bi-Portal radiotherapy, the rate was 4/89 (4.5%) with LDR and 5/65 (7.7%) with HDR. There were no significant differences among these results (Tables 1–3).

Table 1. A comparison between the rates of local recurrence in radical radiotherapy treatments for cervical cancer following Conformation, H-Conformation (conform hollow-out conform radiation) and Bi-Portal (two parallel opposed radiation) therapies.

	Conformation	H-Conformation	Bi-Portal
Low Dose Rate	11/279 (3.9%)	2/43 (4.6%)	4/89 (4.5%)
High Dose Rate	0/0	2/76 (2.6%)	5/65 (7.7%)
Total	10/279 (3.6%)	4/119 (3.4%)	9/154 (5.8%)

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Table 2. A comparison between the rates of local recurrence in radical radiotherapy treatments for cervical cancer following Conformation, Conformation with LDR intra-cavitary irradiation, H-Conformation (conform hollow-out conform radiation) and Bi-Portal (two parallel opposed radiation) therapies.

	1st	2nd	3rd	Total
Conformation	3/50	2/141	6/88	11/279
H-Conformation	0/3	0/19	2/21	2/43
Bi-Portal	0/9	1/49	3/31	4/89
Total	3/62	3/209	11/140	17/411

Table 3. A comparison between the rates of local recurrence in radical radiotherapy treatments for cervical cancer following HDR intra-cavitary irradiation involving H-Conformation (conform hollow-out conform radiation) and Bi-Portal (two parallel opposed radiation) therapies.

	1st	2nd	3rd	Total
H-Conformation	0/4	1/40	1/32	2/76
Bi-Portal	0/7	3/33	2/25	5/65
Total	0/11	4/73	3/57	7/141

The main late complications after cervical cancer irradiation are proctitis and cystitis. However, no patients died because of late complications after radical radiotherapy at our institution. We surveyed all patients who underwent operations because of proctitis or cystitis, or who were given steroid injections for more than 6 months. The rate of local late complications in Conform radiotherapy was 21/279 (7.5%) with LDR; 2/43 (4.6%) with LDR and 8/76 (11%) with HDR in H-Conform radiotherapy, and 7/89 (7.9%) with LDR and 6/65 (9.2%) in Bi-Portal radiotherapy. There were no significant differences among these results (Table 4).

Table 4. A comparison between the rates of late complication in radical radiotherapy treatments for cervical cancer following Conformation, H-Conformation (conform hollow-out conform radiation) and Bi-Portal (two parallel opposed radiation) therapies.

	Conformation	H-Conformation	Bi-Portal
Low Dose Rate	21/279 (7.5%)	2/43 (4.6%)	7/89 (7.9%)
High Dose Rate	0/0	8/76 (11%)	6/65 (9.2%)
Total	21/279 (7.5%)	10/119 (8.3%)	13/154 (8.4%)

## DISCUSSION

The number of patients who underwent radiotherapy decreased over the last 18 years. A decrease in the ratio of Primary Conformation radiotherapy, is apparently responsible for the overall decrease. The most important factor in this decrease has been the development of other treatment modalities, especially chemotherapy. In Nagoya University Hospital, the number of patients undergoing Boost Conformation radiotherapy increased from 1980, but decreased transiently between 1985 to 1989 because of suspicions that increased recurrence was occurring in the field margin. Using magnetic resonance imaging (MRI) and positron emission tomography (PET),<sup>11)</sup> we were able to better determine the extent of residual tumors after irradiation from 1989 onward. As a result of this improved detection, we increased the use of Boost Conformation in 1989 to handle residual lesions.

From 1961, the clinical use of Conform was applied to various kinds of malignant diseases by many doctors at Nagoya University Hospital. The use of a multi-leaf collimator was first reported by Watanabe in 1963.<sup>3)</sup> With this device, the irradiated field could be made to more closely coincide with the target areas, thereby reducing the dose received by healthy organs around the target. A linear accelerator with multi-leaf collimator was first introduced in Aichi Pref. Cancer Center in 1972.<sup>5)</sup> Linear accelerators have a sharp margin, so the dose received by healthy tissue around the target could be reduced even further. The first, collimators were controlled mechanically, a process known as the Conformation Cam Method. Matuda<sup>6)</sup> in 1979 and Ishigaki<sup>7)</sup> in 1983 reported a new method in which collimators were controlled by computer. Obata discussed off-axis irradiation units,<sup>8)</sup> whose collimators could run over the center of the field width. In 1989, a linear accelerator with a variable thickness filter was reported by Kobayashi.<sup>9)</sup> The dose differences emanating from the collimator opening could be compensated for this filter system. In Japan, more than 600 linear accelerators have been manufactured by Mitsubishi, NEC, and Toshiba since 1983, and about 13% of these have a computer-controlled multi-leaf collimator for Conform. Since the second half of the 1980s, 3D treatment plans have become very active.<sup>12,13)</sup> As a consequence, many radiotherapists became more concerned with "conformal radiotherapy".<sup>14-20)</sup> The term "conformal radiotherapy" has a broader meaning than Conform. The conformal technique was applied to static radiation, but Conform is essentially a rotation technique. The "Gamma Knife" is a kind of static conformation radiotherapy.

There are two main aims of conformation radiotherapy. One is to improve of the local control rate, and the other is to protect surrounding radiosensitive organs.<sup>10,21-25)</sup> There have been a few reports about the clinical results of conformation radiotherapy. In 1975, Kakei<sup>26)</sup> reported the clinical results of cervical cancer treated by Conform without intracavitary irradiation. He reported that the rate of local control after Conform was as good as that of local control after treatment by Bi-Portal with intracavitary irradiation with LDR, but the rate of late complications after treatment by Conform was much higher than the local complication rate seen in Bi-Portal. There are no reports about local control or local complications after treatment by Conform with intracavitary irradiation to cervical cancer.

We analyzed the success of Conform in cervical cancer. The absorbed dose of radiotherapy is limited by the tolerance of critical organs in the field. In cervical cancer, the critical organs are the bladder and the rectum. The tolerance dose of the rectum and the bladder is estimated to be about 60 Gy/30 fr/6 w (absorbed dose/fractions/treatment time in weeks). When intracavitary irradiation was from 16 to 24 Gy, the maximum dose of external beam irradiation was about 40 Gy. Using the hollow-out or center-block techniques, the external irradiation dose can be increased to 60 Gy. A higher control rate would be expected following an increase in the dose. In this survey, there were no significant differences among the results. However, we could see a

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trend. As regards to local control, the lowest local recurrence rate was obtained by H-Conform at 60 Gy with HDR in the period 1985 to 1990. Although the local recurrence rate was 2.6% in this period, the late complication rate was somewhat higher at about 11%. With respect to local complications, the lowest rate was about 4.6% obtained using H-Conform of 40 Gy or 50 Gy with LDR from 1983 to 1984. In this period, however, the local recurrence rate was somewhat higher at 4.6%. The results following Conform were between those of H-Conform with LDR and with HDR.

In summary, the rates of local recurrence and late complication following Conform for cervical cancer were lower than those seen in Bi-Portal treatments. Our results showed that Conform combined with intracavitary irradiation lowered the late complication rate below that of Conform alone. H-Conform was not convenient, for hollow-out material had to be customized for every patient. We began to use the center-block technique from 1985. When the conformation technique was used as the first radiation therapy, the entire tumor volume had to include a safety margin. It is difficult to prevent all radiation from reaching the healthy organs near the target area. However, by using the Boost Conformation technique, it is possible to make a small field and thereby minimize the size of the safety margin.

## CONCLUSIONS

First, the number of patients undergoing conformation radiotherapy at Nagoya University Hospital has decreased over the last 18 years. Especially, the number of patients who were treated by conformation radiotherapy as an initial treatment course, decreased. From 1989, the number of patients treated by Boost Conformation radiotherapy increased because residual tumors could be detected by MRI or PET.

Second, the rates of local recurrence and late complication in patients treated by conformation radiotherapy, were lower than the rates associated with Bi-Portal treatment of cervical cancer.

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