Radiation therapy of cancer of the uterine cervix in Northern Ireland

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SUMMARY
From 1976 to 1980, 275 patients with invasive uterine cervical cancer were treated at the Northern Ireland Radiotherapy Centre. Most patients had combined intracavitary and external radiotherapy. Only 26% presented with clinical Stage 1 disease; there were more of these patients aged 30–39.

Five-year survival was 68% for Stage 1, 48% for Stage 2, 16% for Stage 3 and 0 for Stage 4. Survival was better in the age group 30–39 (63%) than in the age group 20–29 (18%) and for those histologically graded as squamous (49%) rather than poorly differentiated (35%). Twelve patients required colostomy. Comparison of these results with other centres in the United Kingdom and the USA show that there is still room for improvement particularly in the identification of early stages of the disease.

INTRODUCTION
For the radiotherapist, cancer of the uterine cervix represents one of the major anatomical sites where treatment is primarily by radiation, and usually undertaken with curative intent. This review describes the population of patients in Northern Ireland and the outcome of treatment over the years 1976–80, during which time it was policy to treat invasive cervical cancer by radiation alone. Only rarely was radiation combined with surgery. When summarised along with two previous reports dealing with the years 1953–60 and 1968–72, the practice of almost three decades is available.

PATIENTS AND METHODS
During the study period 275 new patients were treated at the Northern Ireland Radiotherapy Centre. For three patients there was inadequate initial documentation or early loss to follow-up, and the remaining comments relate to 272 patients. In a small minority, follow-up was completed by use of a specially designed questionnaire. Staging of disease was by clinical examination, almost always under anaesthesia, complemented by intravenous pyelogram, according to the FIGO classification.

With no pretension of systematic histological grading, this study separates those cancers described simply as squamous or moderately differentiated squamous, from those specifically described as poorly differentiated, Grade 3, or anaplastic.

The vast majority of patients had combined intracavitary and external radiotherapy. Intracavitary treatment was according to the Manchester system of...
radium dosage with a central tube and paired lateral vaginal ovoids separated by a washer. No attempt at individual dosimetry was made, and dose calculations depend on the assumption of ideal geometrical distribution. In these patients the radium insertion was of 48 or 60 hours duration, corresponding to approximate Point A doses of 30Gy and 37Gy respectively. When radium alone was used for Stage 1 cases, two insertions totalling 120 hours were employed. External pelvic therapy was delivered on megavoltage equipment (Cobalt 60 or 8MeV linear accelerator). Practice varied slightly between clinicians but generally involved treating the whole pelvis by opposed anterior and posterior fields to 40Gy in 20 fractions over four weeks, or using a four-field pelvic box technique to spare the posterior rectum delivering 40Gy in 13 fractions treating three days per week. There was no uniform policy as to the order in which external and intracavitary treatments were applied. Central pelvic shielding during external therapy was used only occasionally.

RESULTS

Patient numbers and age distribution are given in Table I. Average annual numbers were higher in the period 1968–72 but no obvious explanation was available. There has been no significant change in the age distribution when compared with the two previous reports1,2 and the national figures for 1971.3 The increased incidence of invasive cervical cancer in the youngest age group reported in the NW Thames region4 was not identified in this report.

| Age group | Northern Ireland | England and Wales | NW Thames region |
|-----------|------------------|-------------------|-----------------|
| **Patient numbers** | 520 | 408 | 272 | 4090 | 1175 |
| 20–29 | 0.6% | 2.5% | 11 | 4.0% | 3.1% | 13.5% |
| 30–39 | 10.8% | 5.6% | 27 | 9.9% | 8.8% | 21.6% |
| 40–49 | 28.3% | 26.0% | 47 | 17.3% | 22.7% | 13.6% |
| 50–59 | 28.1% | 31.6% | 78 | 28.7% | 28.7% | 19.2% |
| 60–69 | 21.4% | 20.5% | 70 | 25.7% | 19.8% | 17.4% |
| 70+ | 10.9% | 13.7% | 39 | 14.3% | 17.0% | 14.3% |

In the present study 71 patients had Stage 1 disease, 124 were Stage 2, 67 Stage 3 and 10 Stage 4. There has been a trend towards more patients presenting as Stage 1, from 17% in 1953–60 through 21% in 1968–72 to 26% in 1976–80, but no change in the high proportion presenting as Stage 2 and 3 disease. Within the age groups the stage distribution closely matches the overall pattern except in the 30–39 age group where 16 of 27 patients (59%) presented

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as Stage 1. All the survival statistics given are mature five-year figures representing patients alive and free from disease. This allows direct comparability with previous reports. No patient in this study who was alive and disease-free at five years has subsequently relapsed or died from her disease. Overall, 118 of 272 patients (43%) were alive at five years. Results by stage groups are shown in Table II.

**TABLE II**

*Five-year survival for the group of 272 patients diagnosed 1976 – 80, classified by stage groups*

| Stage   | 1     | 2     | 3     | 4     | Total |
|---------|-------|-------|-------|-------|-------|
| Number of patients | 71    | 124   | 67    | 10    | 272   |
| Died from carcinoma | 16    | 57    | 53    | 10    |       |
| Died from unrelated cause | 8     | 7     | 3     | 0     |       |
| Five-year survivors | 47    | 60    | 11    | 0     | 118   |

(67.6%) (48.4%) (16.4%) 0 43.3%

For the 71 Stage 1 patients, 71% of 39 treated by combined therapy, and 67% of 21 receiving radium alone became long-term survivors. All three patients who had pre-operative radium insertions survived as did three out of six patients who had combined therapy post-operatively. Of the 124 Stage 2 patients, 51% of 103 patients treated with combined therapy survived five years or more. One patient treated pre-operatively survived, as did five out of eight who were suitable for radium treatment alone, but of 12 patients who were only suitable for external radiotherapy only two survived five years.

When analysed by age-group, the only improvement over the average results is in the 30 – 39 group, who had 63% survivors. This relates to the high proportion of Stage 1 cases in this group. Only two of 11 patients aged 20 – 29 survived five years.

Although the allocation of histological grade was not as consistent as would be desirable, percentage survival figures are presented in Table III. There is a difference in survival for those reported as squamous and as poorly differentiated tumours both overall and in Stage 2. This suggests that the histological grade is of prognostic value.

**TABLE III**

*Five-year survival by histological type*

| Histological type  | Overall     | Stage 1     | Stage 2     |
|--------------------|-------------|-------------|-------------|
| Number of patients | 272         | 71          | 124         |
| Squamous           | 80 of 165   | 34 of 47    | 40 of 72    |
|                    | (49%)*      | (72%)       | (56%) +     |
| Poorly differentiated | 29 of 83   | 9 of 18     | 15 of 40    |
|                    | (35%)*      | (50%)       | (38%) +     |
| Adenocarcinoma     | 10 of 24    | 4 of 8      | 5 of 12     |
|                    | (42%)       | (50%)       | (42%)       |

*Chi squared = 5.58, p < 0.05 (with Yates' correction)
+Chi squared = 4.20, p < 0.05 (with Yates' correction)
The late effects of treatment have been assessed only in those patients surviving five years, to exclude confusion between treatment-related morbidity and the symptoms of recurrent or progressive disease. Eighty patients (67%) had predictable treatment morbidity which had completely settled by their first review at two months. In 17 (14%) symptoms persisted for up to one year. Fifteen of the survivors (12.6%) suffer at least occasionally from symptoms mainly of rectal irritation, and seven (5.9%) have a permanent colostomy. Within the entire group of 272 patients there were five further colostomies in patients who ultimately died from their disease, giving an overall colostomy rate of 4.4%. Of the 12 patients requiring colostomy, seven had received the higher intracavitary dose of 60 hours radium with 40Gy pelvic irradiation, three followed double intracavitary insertions and two had had pelvic irradiation by suboptimal regimens.

**DISCUSSION**

This report demonstrates the results achieved in routine treatment of cervical cancer in Northern Ireland. While the five-year survival figures bear comparison with other UK results at the same period of time they undoubtedly fall below current expectation where the anticipated cure rates would be 80% in Stage 1, 60% in Stage 2 and 30–40% in Stage 3. The survival times for patients treated by radiotherapy for several major centres are shown in Table IV.

It would be unrealistic to seek increased cure rates simply by increasing the radiation dose, which would cause a disproportionately greater increase in morbidity. Policy changes incorporated in current technique will, it is hoped, result in a reduced morbidity with no loss of disease control. These changes
### TABLE IV

**Survival comparisons (per cent) for patients treated by radiotherapy**

| Stage | 1  | 2  | 3  | 4  |
|-------|----|----|----|----|
| Northern Ireland |     |    |    |    |
| 1953 – 60 | 57% | 46% | 25% | 12% |
| 1968 – 72 | 69% | 46% | 26% |    |
| 1976 – 80 | 68% | 48% | 16% |    |
| United Kingdom |     |    |    |    |
| Royal Marsden | 1962 – 70 | 74% | 46% | 16% | 6% |
| Manchester | 1961 – 65 | 73% | 52% | 25% |    |
| Cardiff Cathetron | 1974 – 77 | 77% | 50% | 25% |    |
| USA |     |    |    |    |
| Patterns of Care Outcome Study |     |    |    |    |
| All centres | 87% | 66% | 28% |    |
| Major centres | 92% | 77% | 60% |    |
| Worldwide |     |    |    |    |
| 118 institutions; 26 countries | (1959 – 63) | 77% | 56% | 32% | 9% |

include adoption of a manual afterloading system of intracavitary treatment with caesium 137 in place of radium which allows improved positioning and packing. A fairly modest Point A dose of 32Gy is given from the intracavitary treatment. External radiotherapy is given in conventional daily fractions of 2Gy and central pelvic shielding is used more often during the last quarter of the external treatment. If these improvements produce lower morbidity levels at no expense in cure rates, then increased dosage could be applied. Radical hysterectomy has been revived in the 1980s for selected Stage 1 cases in younger patients, and results of this operation will require close comparison with conventional radiotherapy.

The findings indicate that patients treated for this disease in Northern Ireland are very similar to those in the rest of the UK in terms of age, stage at presentation, histology and outcome. In the under-30 age group described here, the poor survival is closely related to relatively advanced stage at presentation and worse than average histology. A similar poor survival in young patients was also noted in patients treated on the Cathetron at the Middlesex Hospital. Here relapse-free survival in the over-35s was 87% compared with only 17% in the under-35s. Such data adds to the current debate as to how best to screen and treat these young patients who suffer from what appears to be a particularly aggressive disease.

The impact on prognosis of the histological grade, despite the absence of any systematic approach in the Northern Ireland data, suggests that this aspect should be more closely investigated.

Two major aspects of control failure are seen. First the problem of achieving local control in bulky Stage 2 and Stage 3 presentations, and the more unpredictable group of patients who can achieve local pelvic control, but whose disease behaves
with a more aggressive metastatic tendency. The first problem can be dealt with, as most commonly in the USA, by considerable increase in the total pelvic treatment dose but this will produce major morbidity rates greater than 20%. Experience in the UK of acute and late complications of such increased dose render this policy largely unacceptable. The second, or indeed either group, could theoretically benefit from chemotherapy for bulk reduction or eradication of occult metastases. Experience with existing agents in advanced or recurrent disease shows that only a minority of patients demonstrate any response and that very few get a complete response which even then cannot be maintained. There seems no place at present for the routine incorporation of toxic chemotherapy in the primary management of cervical cancer. More productive will be the enhancement of programmes to detect the disease at its earliest stage to ensure control by proven local measures.

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