

1. Introduction

Background and Aim

The SBU report "Radiotherapy for Cancer" was published in 1996. That report addressed the role of radiotherapy for treating tumours. It described the current use of radiotherapy in Sweden 1992, reviewed the scientific literature on radiotherapy up to 1993, and estimated the costs associated with radiotherapy. It was the first evidence-based analysis of radiotherapy and the results have attracted considerable attention both in Sweden and abroad. Since then, several important studies have been published and the technical development of radiotherapy has been considerable. Hence, there was a reason to review the recent scientific literature and determine the extent to which the new findings affect the conclusions presented in the earlier SBU-review. Furthermore, it was found important to assess if the conclusions in the report had lead to changes in clinical practice.

The scientific literature on radiotherapy for tumours that has been published since the previous report has been surveyed and evaluated. The primary questions to which answers were sought in the literature review were:

1. Is radiotherapy beneficial for the tumour diseases in question?
2. If so, what type of radiotherapy and on what scale?

Questions and Limitations

The literature review was primarily geared to routinely used external radiotherapy and brachytherapy. All forms of cancer which were considered in the previous report are included in this update, which also takes in urinary bladder cancer and the oesophageal cancer.

The search period for the update of the old sections comprises the time from 1994 onwards. For the additional cancer forms the search generally comprises the same period, but it also covers the last ten years as

regards randomised controlled studies and systematic literature reviews. The backward limit to the search is based on the requirement that the studies should reflect modern radiotherapy techniques and allow a sufficiently long follow-up of the patients.

The minimum level for the studies that have been evaluated, generally speaking, requires systematic reviews, randomised controlled studies, and, if relevant, other controlled studies.

Evaluation of the Literature

The literature search was performed in relevant databases. The databases in question, the limitations, period and search words are presented in each chapter.

The resulting studies have been examined and sorted in three phases:

Phase 1 Sorting via lists and article summaries

Two members of the group independently studied all the abstracts from the search. Abstracts which both reviewers considered irrelevant were sorted out. Relevant abstracts and those considered doubtful went on to phase 2.

Phase 2 Examination of full-text articles

Complete articles were ordered on the basis of the abstracts. Articles which did not satisfy the set criteria or did not focus on the relevant problem were sorted out.

Phase 3 Critical examination of selected studies

The examination followed a special template for assessing the quality and extracting data.

Classification and Evaluation

The scientific studies have been assessed according to the same system as used in the previous report on radiotherapy. It consists of two components: (1) a classification of the study based on the type of study and (2) an evaluation of the scientific quality of the study.

The classification comprised the following types of studies:

- *Meta-analyses (M)*. A statistical synthesis of several randomised studies. The meta-analysis can be based on original data from the studies, or solely on information reported in the literature.
- *Phase III studies (C)*. Prospective studies that randomise among alternative treatment methods or between treatment versus control. May be broadly designed, and involve the participation of multiple centres/ departments – multicentre studies – or they may be conducted at a single department. The quality of these studies depends on whether the patient data is sufficiently large to permit valid findings, and on the external and internal validity of the findings.
- *Phase IIII studies (P)*. Prospective studies, usually non-randomised, which follow a well-defined protocol. Often used to study the side effects and effectiveness of new treatment. These studies require fewer patients.
- *Retrospective studies (R)*. Retrospective studies analyse patient data that are usually collected at a particular department over a longer period, or collected from different centres in an international database. Treatment often varies over time. Large, closely monitored patient studies with long follow-up times that are subjected to adequate statistical analysis can be of substantial value.
- *Review (L)*. Review articles, such as literature reviews or chapters in textbooks/reference books. May contain detailed accounts of reported studies, but may also be more general in nature.
- *Other articles (O)*. This category includes case studies, letters to journals, editorial comments, etc., and summaries from scientific meetings. Animal experiments and technical reports also fall within this category.

The evaluation was carried out for each study as regards its scientific quality by type of study as defined above according to a three-stage scale: high, moderate, and low. Hence, the proportion of high quality studies listed in the tables is high. The definition of these categories for each type of study is stated in Table 1.

Table 1 Principles for classification of literature.

| Type of Study*) | Scientific Quality = Weight of the Evidence | | |
|-----------------|--|--------------|--|
| | 1 = High | 2 = Moderate | 3 = Low |
| M | Thorough reanalysis of well-defined original data from all studies. | | Summary based on a few studies and/or solely on reported findings. |
| C | Large, well-monitored multicentre studies that adequately describe protocols, patients, and methods including treatment methods. Patient data sufficiently large to address the issue. | | Randomised studies with too few patients and/or too many arms, yielding insufficient statistical power. Poor accounting of the data, high drop-out. Poor description of treatment methods. |
| P | Well-defined issue, sufficient patient data, adequate statistical methods. | | So-called “quick-and-dirty” studies. |
| R | Large, consecutive patient data that are well defined and analysed by adequate statistical methodology (e.g multivariate analysis, case-control methods, etc). Long follow-up period. | | Limited patient data. insufficiently defined, inadequate follow-up time, inadequate statistical methods. |
| L | Thorough literature review, well-documented patient data often presented in table form. | | Reports with incomplete reference citations and poorly supported conclusions. |
| O | High-quality textbook chapters | | |

*) M = Metaanalysis; C = Prospective and randomized study; P = Prosepective study, not randomized
R = Retrospective study; L = Review; O = Other article

The study category and the weight of evidence are stated in brackets after each reference in the literature chapters. These characteristics are also summed up at the end of each chapter or section, as exemplified in Table 2 and 3.

Table 2 and 3 show the classification and evaluation of all the scientific articles on which the previous and the present reports are based:

Table 2 The articles on which the conclusions in the earlier report were based were classified and graded as follows (number of studies/number of patients).

| Type of study | 1 = high | 2 = moderate | 3 = low | Total |
|---------------|--------------------|--------------------|-------------------|----------------------|
| M | 4/82 181 | 9/37 478 | – | 13/119 659 |
| C | 105/50 855 | 108/25 038 | 54/9 302 | 267/85 195 |
| P | 79/7 133 | 94/5 602 | 27/33 830 | 200/46 565 |
| R | 219/386 017 | 355/34 255 | 214/11 965 | 788/432 237 |
| L | 142/25 122 | 55 | 3 | 200/25 122 |
| O | 106/592 | 80/418 | 12 | 198/1 010 |
| Total | 655/551 900 | 701/102 791 | 310/55 097 | 1 666/709 788 |

Table 3 The articles on which the conclusions in this report were based were classified and graded as follows (number of studies/number of patients).*)**)

| Type of study | 1 = high | 2 = moderate | 3 = low | Total |
|---------------|--------------------|-------------------|-------------------|--------------------|
| M | 15/62 107 | 7/24 207 | 1/– | 23/71 833 |
| C | 88/41 949 | 86/17 924 | 133/18 178 | 307/59 827 |
| P | 33/4 900 | 37/3 399 | 29/816 | 99/9 115 |
| R | 37/34 165 | 49/7 445 | 32/2 676 | 118/44 356 |
| L | 44/799 | 7/– | 3/– | 54/799 |
| O | 31/64 | 6/– | – | 37/64 |
| Total | 248/124 156 | 192/44 987 | 198/16 851 | 638/185 994 |

*) Since some patients can be included in several reports, the sums of the total are lower than the sums of the numbers given within the table.

**) Prostate Cancer not included.

Level of Evidence for Conclusions

When all the relevant studies had been examined, the weight of the scientific evidence was summed up in a number of concluding statements for each type of tumour. The editor has put an extensive effort and amount of work into harmonizing the weight of evidence of the conclusions and expressing them in a uniform way. For example, if a conclusion is said to be based on strong evidence, this implies randomised, controlled studies or metaanalyses of high quality. However, this method implies that the stated weight of evidence of the conclusions is not in concordance with the definitions (evidence level 1–4) used in more recent reports from SBU.

Working Methods

A project group has had the ultimate responsibility for the update. The project group appointed a literature group. The literature group appointed a chief reviewer and some referees for each chapter. The chief reviewer produced the draft of a text which was then scrutinised by the referees, and adjusted if necessary by the chief reviewer. One person (Eva Cavallin-Ståhl) had the final responsibility for the content of the literature studies and for editing the texts according to agreed templates.

Four international experts have had the task of scrutinising the literature study in the final phase. It has also been examined by three external Swedish reviewers, appointed by the SBU Scientific Advisory Group. The literature study underwent a final examination by the SBU Scientific Advisory Group and the SBU Board.