Brachytherapy for prostate cancer

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Authors' objectives
To review the effectiveness of brachytherapy for prostate cancer.

Searching
MEDLINE (1997 to Aug 1999, the Cochrane Library (latest version), Cancerlit (1997 to Aug 1999), EMBASE (1997 to April 1999), HealthSTAR (1992 to Aug 1999) and CINAHL (1997 to April 1999) were searched (search terms listed). In addition, the reference lists of retrieved articles were searched. Information about prostate cancer and brachytherapy was also obtained by searching the World Wide Web. No language restrictions are reported.

Study selection
Study designs of evaluations included in the review
Study designs comparing brachytherapy with other therapeutic approaches were preferred. Study designs reported in the review include: controlled trials, prospective and retrospective studies.

Specific interventions included in the review
Brachytherapy (a radiotherapy technique that involves placing radioisotope seeds into, in this case, the prostate gland) either used alone or in combination with other therapies such as neoadjuvant androgen deprivation therapy, external beam radiotherapy (EBRT). The studies reported in the review included the following radioisotopes for brachytherapy, either alone or in combination: 103Pd, 125I, 192Ir and 198Au. Comparators included: radical prostatectomy, conformal external beam radiotherapy.

Participants included in the review
Patients with prostate cancer (various clinical stages of disease and previous treatments).

Outcomes assessed in the review
Studies reporting patient outcomes (not specified) were preferred. Outcomes reported in the review include: biochemical outcomes (prostate specific antigen levels), clinical outcomes (DRE, biopsy, bone scans, CT scans), survival and complications.

How were decisions on the relevance of primary studies made?
The results of the literature search were first screened by title, then by abstract and the literature thought to be more relevant was then obtained. The authors do not state how many of the reviewers performed the selection.

Assessment of study quality
The authors do not report any a priori formal assessment procedure. However, the quality of the studies and the evidence is discussed in terms of study design (e.g. method of allocation, use of control group, selection of patients, length of follow-up etc.). The authors also make some comment in the results section to the classification system of Jovell and Navarro-Rubio (see Other Publications of Related Interest no.1), though individual studies are not discussed. The classification system of Jovell and Navarro-Rubio mentioned by the authors graded evidence from meta-analyses of RCTs or from large RCTs as 'good'; small RCTs and non-randomised controlled trials as 'good to fair'; non-randomised controlled retrospective studies, cohort studies and case-control studies as 'fair'; and non-controlled and other studies as 'poor'.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. Tables reported in the review include the following types of information: bibliographic details, participant...
Methods of synthesis
How were the studies combined?
A narrative synthesis was used.

How were differences between studies investigated?
Differences between studies were not formally assessed but some differences were discussed.

Results of the review
Twenty-three studies (n=6678 participants) were included. Sixteen of the studies were retrospective, three prospective, two further potential prospective studies, one treatment programme and one pilot study. Seventeen studies were included in the assessment of complications (n=2928).

Biochemical outcome measures (e.g. PSA):
The majority of studies used the level of prostate specific antigen (PSA) in the blood as an outcome measure. However, the use of this outcome measure is controversial and it may not be a reliable indicator of response to treatment. In the short-term, PSA levels appeared to favour brachytherapy, especially amongst low risk patients. Similarly, brachytherapy combined with EBRT showed short-term improvements. However, both sets of evidence were mainly from uncontrolled or retrospective studies. Of the three studies comparing different treatment modalities, none found any major statistically significant differences between brachytherapy and other treatments.

Clinical outcome measures (e.g. digital rectal examination (DRE), biopsy, bone scans, CT scans):
The results of these studies mirror those of the biochemical studies, but suggest that such outcome measures are less sensitive than clinical methods at detecting recurrence.

Overall survival (n=10 studies):
Due to the relatively short period of follow-up in many studies, survival was often not reported. Only ten studies reported cancer death rates for brachytherapy patients and these were in the 2-3% range with the exception of one study, which showed significantly higher rates. However, this study dealt with recurrent disease.

Complications (n=17 studies):
Complications associated with brachytherapy included mild acute urethritis and proctitis for most patients. Long term complications were restricted to a low percentage of patients and were similar or lower than was observed for EBRT or RP treated patients. Few studies reported effects in terms of impotence. Only one retrospective study directly compared two treatment modalities and this favoured brachytherapy versus CRT. The authors of this study commented that the higher radiation dose in CRT seems to be a risk factor for impotence compared to brachytherapy.

Quality of evidence:
There was a lack of controlled trials, and incomplete reporting, limited comparisons with other treatment modalities, inadequate outcome data and difference in study populations make the assessment of evidence difficult. The methodological quality of the studies in terms of the classification of Jovell and Navarro-Rubio was fair for short-term biochemical survival, but poor for overall survival and complications.

Authors' conclusions
The present report confirms that brachytherapy appears a promising intervention in the short term. However, its potential for influencing overall outcomes, particularly long term morbidity and survival, are unknown. Patient selection
issues discussed in the report make the prediction of its eventual effectiveness problematical. It is possible that there may be some bias in the existing reports towards selection of more promising candidates for treatment.

CRD commentary
This review was based on a reasonable search of the literature. However, no attempts were made to locate unpublished data so publication bias may be a problem. In addition, the inclusion/exclusion criteria were not always clearly defined a priori. Details of the methodology of the review were also lacking (e.g. how many reviewers were involved in selecting, extracting and assessing the quality of studies). Although they do discuss certain methodological issues and make reference to the quality of the evidence with respect to a defined set of criteria, the quality ratings of individual studies was not presented. Other details of study design and reporting were however reported adequately in tables.

Considering the variety of study designs, populations and interventions, the use of a narrative synthesis was appropriate. The authors discuss some of the differences between the studies in the text of the review. Overall, given the data presented, the findings and implications of the review would appear to be reasonable.

Implications of the review for practice and research
Practice: The authors state that there is fair evidence for the short-term biochemical survival of patients treated with brachytherapy, but poor evidence for effects of treatment on overall survival and for complications.

Research: The authors state that long-term good-quality randomised controlled trials are required to definitively establish the efficacy of brachytherapy for prostate cancer. In addition, comparative information on the safety of different modalities of brachytherapy is required.

Bibliographic details

Original Paper URL

Other publications of related interest

Indexing Status
Subject indexing assigned by CRD

MeSH
Brachytherapy; Male; Prostate-Specific Antigen; Prostatic Neoplasms /radiotherapy

AccessionNumber
12000008193

Date bibliographic record published
31/05/2001

Date abstract record published
31/05/2001

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on
the reliability of the review and the conclusions drawn.