Randomized trial of high- and low-source strength (125)I prostate seed implants

Narayana V, Troyer S, Evans V, Winfield R J, Roberson P L, McLaughlin P W

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of permanent prostate implants of high- and low-source strength seeds for the treatment of localised prostate cancer was examined. The high-source strength seed was 0.76 microGrays/metre squared (microGy/m2) per hour. The low-source strength seed was 0.4 microGy/m2 per hour.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who were candidates for permanent prostate implantation. No inclusion or exclusion criteria were described.

Setting
The setting was secondary care. The economic study was carried out in Michigan, USA.

Dates to which data relate
The study year was not provided. The price year was not stated.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The resource use data were based on the same patient sample as that used in the effectiveness study, and were collected prospectively.

Study sample
No power calculations or methods of sample selection were reported. There was no report of patients refusing to participate or of patients excluded for any reasons. There was also no demographic information or descriptions of health status, beyond prostate volume. Forty patients were randomised, 20 to each arm. Five patients in each arm received brachytherapy alone and 15 received combination therapy with external beam radiotherapy.

Study design
The study was a randomised controlled trial that was conducted in a single centre. The patients were randomised according to the week they received treatment, but the number of weeks over which randomisation took place was not reported. The patients were followed up 2 weeks after implantation. No loss to follow-up was reported. The study does not appear to have been conducted blind.

**Analysis of effectiveness**

It appears that the analysis of effectiveness has been conducted on an intention to treat basis, but the poor reporting of the study inclusion and exclusion procedures makes this difficult to confirm. The primary health outcome was an index of achieved dose over ideal planned dose. This was measured using MRI-based dosimetry and CT-based dosimetry. The D99, D95, D90 and D80 indices (dose received by respective percentage of prostate gland) were calculated. In addition, the isodose distributions and the dose-volume histograms were also calculated. Patients in each arm were shown to be comparable in terms of prostate volume, but no other information on comparability was provided. There was no adjustment for possible confounding variables.

**Effectiveness results**

Except for D80, the planned dose to the ultrasound prostate in the two arms was similar. The ratio of D80 to the prescription dose showed a statistically significant difference, (p=0.02), between the high-source strength arm (1.5 +/- 0.1) and the low-source strength arm (1.4 +/- 0.1).

The ratio of the prescription isodose volume to the ultrasound prostate volume was greater for the high-source strength arm (2.21 +/- 0.43) than for the low-source strength arm (1.88 +/- 0.24), (p<0.0001).

The planned V200 (percentage of volume receiving 200% of prescribed dose) was, on average, 33.2% (+/- 9.8) for the high-strength arm and 25.4% (+/- 8.3) for the low-strength arm. The difference was statistically significant, (p=0.01).

For the achieved dose to prostate, a statistical significant difference was found between the two arms for each dose index, with a greater index for the high-source strength arm using CT and MRI dosimetry.

There was no statistically significant difference for the planned/achieved ratio of V200.

The V100, V150 and V200 were statistically significantly greater in the high-source strength arm than in the low-strength arm.

All dosimetric end points for MRI-based dosimetry were lower than those for CT-based dosimetry.

No statistically significant differences were found in the two arms for the dose to rectal wall and the dose to urethra.

No statistically significant difference was observed in swelling between the high-source strength arm (1.13 +/- 0.2) and the low-source strength arm (1.20 +/- 0.2).

**Clinical conclusions**

The authors concluded that high-source strength implants are better quality than low-source strength implants.

**Measure of benefits used in the economic analysis**

No summary health benefit was used in the economic analysis. In effect, a cost-consequences analysis was performed.

**Direct costs**

The resource use quantities were reported separately from the costs. The study included only the cost for each seed. Operating room time was estimated for each treatment arm, although the associated costs were not included in the cost analysis. The unit cost was based on the authors' estimate. Discounting was not relevant given the short follow-up period of the study (2 weeks). The study reported the average costs. The price year was not reported.
Statistical analysis of costs
No statistical analysis of the costs was undertaken. The study provided only a rough estimate of seed cost, thus a detailed analysis was not possible.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was not required, given that sample data were available for the effectiveness evidence.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The study estimated that if each seed cost $40, the total seed cost was $2,400 per case in the high-strength arm and $3,840 per case in the low-strength arm. The study did not include any other costs. Discounting was not relevant.

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
The high-source strength implants provided higher quality at lower cost in comparison with the low-source strength implants.

CRD COMMENTARY - Selection of comparators
The choice of the comparators was based on current practice for localised prostate cancer in the study setting. You must consider whether permanent seed implantation is a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a prospective randomised controlled trial, which is appropriate for the study question. The poor reporting of the methods used to select the sample made it difficult to determine the quality of this non blinded study, which may have been low. It was unclear whether the study sample was representative of the study population. The lack of demographic data and information about co-morbidities mean that the generalisability of the results cannot be objectively assessed. The patient groups were not shown to be comparable at analysis, except in terms of prostate volume. The failure to report the comparability of the patient groups and any potential confounding factors, combined with the poor quality of the sample selection process, represent the main drawbacks of the study. Therefore, the internal validity of the results was unclear.

Validity of estimate of measure of benefit
The authors did not derive a measure of health benefit. The analysis was therefore categorised as a cost-consequences analysis.
Validity of estimate of costs
The authors did not state any cost perspective, and only a cursory cost estimate (an estimated seed cost) was included in the analysis. Therefore, the study would appear inadequate for assessing the resource use associated with the technology under evaluation. A complete analysis should also include the costs of the operation and any follow-up treatment. However, it appears that the conclusion that high-source strength implants are less costly than low-source strength implants might not have been unreasonable if the cost of each seed is identical and the lower number of high-source strength seeds reduces the operating time. Resource use was reported separately based on observational data. The costs and the quantities were reported separately, which may aid the reproducibility of the results. The year to which the prices referred was not stated and this limits the generalisability of the results.

Other issues
The authors did not compare the results of their study with findings from other studies. This may have been because the study was terminated early on account of planning implications highlighted from the use of MRI-based dosimetry. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively, but the lack of detail about the patient sample inhibits the interpretation of the results. The authors did not report any further limitations of the study.

Implications of the study
The authors did not make any explicit recommendations for changes in policy or practice. No further research was explicitly identified.

Source of funding
None stated.

Bibliographic details

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MeSH
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