Radiotherapy in bone metastasis : the Dutch bone metastasis study

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Impact of randomized trial-outcome in the treatment of painful bone metastases; patterns of practice among radiation oncologists. A matter of believers versus non-believers?

Editorial

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Department policy, previous training, and tradition seem to be very strong determinators for treatment preferences and may hamper the acceptance and implementation of the results of clinical trials.

This problem is probably as old as medical science itself. When renaissance scientists started to study the anatomy using the human corpse instead of animal corpses as Galen had done, the great Silvius wrote; '... if what the eye sees at dissections does not correspond with what Galen has reported, the fault lies not with Galen but with the corpse'.[1] Also, the papers by Wong et al,[2] Roos[3] and Lievens[4] et al clearly demonstrate the low acceptance of the extensive literature on the successful use of single dose radiotherapy for painful bone metastases. An issue which also during recent years have been given high priority in this journal.[5-11] Wong et al [2] sent a survey to 300 radiation oncologists in Canada presenting 5 case-scenarios, which were also used in two earlier USA surveys.[12,13] Fifty-seven percent of the questionnaires were returned. Most Canadian radiation oncologists (64%) used 20 Gy in 5 fractions. Only 17% used a single fraction. The authors conclude that in spite of the outcome of randomized trials, in which single dose radiotherapy was equally effective as fractionated radiotherapy in the relief of pain, there have been no changes in the treatment regimens in Canada. It is interesting that the authors themselves recommend an individual approach taking into account the extent of the disease, the histology and the performance status. They thus ignore the outcome of the large Dutch trial, in which no difference was found in single versus fractionated radiotherapy in 1171 randomized patients.[14] Roos[3] distributed a survey form to 114 radiation oncologists who visited the October 1998 meeting of the Royal Australian New Zealand College of Radiologists Annual Scientific Meeting, using almost the same clinical cases as in the previously published surveys in Europe, Canada and the USA.[12,15-18] Forty-six percent of the attendants responded. Single fractions were given in only 42%, 28% and 15% of patients with bone metastases of lung-, prostate- or breast-cancer. The Australian New Zealand TROG 96.05 study is currently investigating the importance of the treatment schedule on neuropathic bone pain. An interim analysis showed a 60% overall response rate.[19] Completion of this trial is awaited.

Both Wong and Roos note that reimbursement may be a contributing factor in the decision making process. Wong et al [2] refer to the publication of Ben-Josef et al;[12] Roos[3] refers to the surveys of Lawton et al,[17] Maher et al[18] and Duncan et al.[16] They all indicate that longer schedules are favored in private practice.

In this respect the two papers by Lievens et al [4,20] in this journal are of great interest. The authors sent two questionnaires (about reimbursement and palliative radiotherapy practice) to 565 centers in 19 European countries found in the 1997 ESTRO directive. Thirty percent returned both questionnaires. Subgroups were formed on the basis of department size, country, type of

department (e.g. university vs. private) and reimbursement system (e.g. budget vs. case-payment vs. fee for service and combinations of these). They conclude that larger centers use shorter schedules and less complex treatments. University centers more often use hypofractionation. Is this because they are often (but not always) larger, because they often (but not always) have a budget reimbursement system, or because they are more inclined to accept results from clinical trials? The Australian and New Zealand colleagues who did change to single fractionation cited literature results as the main reason for changing.[6] In their two papers Lievens et al[4,20] suggest that the reimbursement system has its influence on doctor's behavior, although there might be some reluctance to accept this openly. They found a statistically significant relationship between the fractionation schedule or the use of shielding blocks and the reimbursement system. There was a trend between the use of isodose calculations or the field set-up and the reimbursement system. It is hard to believe that these facts coincide with training, tradition and department policy, or are the basis for it. The best way to test the hypothesis whether a reimbursement system has an influence on treatment preferences is to see whether a change in treatment policy occurs, independently from other factors, after a change in the reimbursement system. The announced change of the Belgian reimbursement system seems to offer such an opportunity.

What happened in the Netherlands after the completion of the Dutch Bone Metastases Study? First we believe that the Dutch trial [14] can meet all the criticism expressed by Ratanatharathorn et al.[21] Almost 1200 patients were randomized, which is sufficient to take care of all known and unknown variables. Also this group of patients is representative for the general population meeting the entry criteria, which is proven by the registry study. More than 3000 patients with bone metastases were registered during the study. Reasons for not participating are known in detail. The follow up was substantially longer than in most other studies. One year after randomization 205 patients still sent in their questionnaires. Others were too ill or had already died. Patients with a suggested favorable prognosis were stratified and separately randomized. The comparison of the two strategies including re-treatment, showed no difference between the two arms: not for histology, not for site of metastasis and not for prognosis. In the 1x 8 Gy group there was 25% re-treatment vs. 7% in the 6x 4 Gy group. If single fraction radiotherapy is used, this higher chance on retreatment seems to be the price for a lower treatment burden for both patient and hospital. Not so much an insufficient first single irradiation but the doctors' opinion on expected effectiveness and tolerance after a single dose seems to be the largest contributing factor in this higher chance on retreatment.

At a recent meeting in March 2000 of the Dutch Society for Radiotherapy and Oncology (NVRO) we questioned the radiation oncologists present about whether the outcome of the Dutch Bone Metastases Study changed the treatment schedule from fractionated to single dose. Before outcome of the results most institutes used a multiple fraction treatment schedule. In the meantime almost all 21 Dutch institutes have changed (or are planning to change) their protocols from fractionated to single dose irradiation. This states that in a relatively small and well-organized country as the Netherlands conclusions on a specific subject are drawn and implemented.

Clinical trials are performed to lead to a better or different care. We postulate that when evidence based medicine is performed the patient will benefit most, not only because the treatment outcome is good, but also because the treatment time and waiting lists are shorter. Saving of radiotherapy capacity is considered the major economic advantage of single dose schedules. [14] The type of reimbursement should have little influence on doctors' decisions in the use of a specific treatment schedule.

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Eénmalige bestraling van pijnlijke botmetastasen even effectief als meervoudige bestraling. Uitkomsten van de Nederlandse Botmetastasen Studie

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