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### The accuracy of prostate radiation therapy using a fiducial point-pair registration technique based on a computer assisted portal imaging quality assurance program - PIP-Spro.

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**Purpose:** Portal imaging is a useful tool in external beam radiotherapy for quality assurance of patient positioning. We present a retrospective portal imaging study of the patient positioning variability in the treatment of prostate cancer patients treated with whole pelvic irradiation followed by arc therapy or boost fields (Serie I), and patients treated by "small" pelvic box technique (Serie II).

**Methods:** Weekly APPA and Left-lateral portal images were compared to simulation films by using a fiducial point-pair registration technique based on a computer assisted portal imaging quality assurance program, PIP-Spro, developed specifically for the verification of treatment positioning in radiation therapy.

**Results:** Serie I with 194 portal films (97 APPA and 97 Lateral) of 34 patients treated by whole pelvic irradiation were analyzed. Overirradiated (OA) and underirradiated (UA) areas were computed in terms of percentage of the reference field size. The averaged OA was 2.75% and the averaged UA was 2.74% in APPA portals. For lateral portals an OA of 2.49% and a UA of 2.78% were obtained. Serie II with 194 portal films (98 APPA and 96 lateral) of 25 patients treated with small fields box technique were analyzed. The average OA was 0.88% and average UA 0.86 in APPA portals, and 1.03% and 0.82% for left lateral portals respectively.

**Conclusion:** The accuracy of patients positioning in irradiation of prostate cancer in our institution is in the range of 2.5% for pelvic field technique, and 1.0% for the small field technique. PIP-Spro is an effective useful tool to quality assurance in radiotherapy.

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### Quality of life assessment after definitive radiotherapy of prostate cancer

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**Purpose:** To assess the appearance and severity of sequelae after definitive external beam radiotherapy (EBRT) for prostate cancer by questionnaire.

**Material and methods:** 38 patients with localized T1-4N0M0 prostate cancer, underwent definitive EBRT with or without hormonal treatment (HT). Patients with T3,4 tumor, had pelvic irradiation and conformal prostate boost (mean 68.6Gy), patients with T1-2 tumour had prostate EBRT only by 3D conformal technique (mean 68.9Gy). 19 of 38 patients had no, or neoadjuvant HT before and during the EBRT (H- group), and 19 patients had long term HT, which lasted by the time of the survey (H+ group). 7-26 months (mean:14,1) after the end of EBRT patients were interviewed on the incidence and severity of bowel, urinary and sexual functions. They scored 0 to 4 for normal function to severe dysfunction (type A question). They also scored the change in the status. Scores -1 to 2 meant that the function was: -1: better, 0: the same, 1: worse, 2: markedly worse at the time of the survey than it had been before the EBRT (type B question).

**Results:** On type A questions, the mean scores of difficulty, frequency and leaking on urinating were 0.10, 1.31 and 0.56. Scores of frequency, loose and painfulness of stools were 0.25, 1.21 and 0.28. Scores of libido and erectile function were 2.48 and 2.28. On type B questions, the mean scores of different urinary functions were -0.13, -0.05, -0.05. Mean scores of bowel functions were: 0.33, 0.46, -0.03. Mean scores of libido and erectile function were: 1.08 and 1.00. In the two groups of patients (H+ vs. H-) the mean scores of different urinary functions were comparable as 0.11 vs. 0.11, 1.26 vs. 1.37 and 0.42 vs. 0.68. Different bowel function were scored as 0.16 vs. 0.37, 1.05 vs. 1.37, and 0.37 vs. 0.21. Libido and erectile function scores were 3.05 vs. 1.95 and 2.89 vs. 1.74.

**Conclusions:** Urinary and bowel symptoms were tolerable. Mean scores showed only mild deterioration of these functions. Decrease in sexual function was the most disturbing sequelae influencing patients, quality of life. Long term hormonal manipulation had no effect on urinary and bowel symptoms but made the sexual functions markedly worse comparing to neoadjuvant hormonal treatment.

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### The impact of early post-implant prostatic oedema on prostatic dimensions where temporary high dose rate (HDR) brachytherapy (BT) boost is administered via flexiguide needles for prostatic cancer.

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**Purpose:** To demonstrate whether oedema induced by the trauma of temporary BT flexiguide needle placement plus the administered BT irradiation significantly affects prostatic dimensions over the 1-2 days duration of a temporary implant where usually 4 increments, given twice daily, were administered.

**Materials & Methods :** Four patients treated with HDR-BT boosts were analysed by each having 2 successive CT scans : the first within 4 hours of needle placement and the second just prior to needle removal. The time between scans ranged from 23.5 to 49.5 hours. The effect of oedema on flexiguide needle displacement was best assessed in the transverse plane in which all needles were visible and which was most distant from the template, ie least hindered by template proximity and rigidity. Utilising methods based on Waterman et al , the mean radial distance of each needle position from the geometric centre of each implant (MRD), the changes in MRD between each pair of CT scans, and thereby the relative change in prostate volume over the duration of each implant was calculated. The influence of oedema on the cranio-caudal axis was negated because of the use of effectively linear sources along the needles paths, and because the active length adequately covered the superior and inferior extent of the prostate on each pair of CT studies.

**Results:** The change in MRD between CT studies ranged from +0.21 to -0.97mm ie +1.55 to -5.39% for the 4 cases, respectively and a range of +4.7 to -18.0% in prostatic volume.

**Conclusion:** Within the time of the temporary implant, competing influences of increasing and resolving traumatic oedema and BT induced oedema occur. Unpredictable changes in prostatic volume result. In 3 of 4 cases analysed the volume changed from -1.5% to +5.6% and dosimetry was unaffected. The fourth case, was technically difficult and more traumatic with multiple needle passes. Immediate post-implant oedema was excessive and 18% reduction in prostatic volume over implant duration occurred resulting in significant dosimetric impact. In such traumatic BT implants, repeat dosimetry may need to be considered prior to the second day of fractionated HDR.

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### Radiation and hormonal therapy in the treatment of prostate cancer

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**Purpose:** The purpose of these studies is to evaluate the results of treatment of 188 patients with prostate cancer in different stages.

**Methods:** This paper reviews 188 patients with prostate cancer treated at the Institute of Radiotherapy and Oncology Skopje in the period from 1989 to 1999. The patient were in different stages of disease (AUA Classification): 36 (19%) in Stage B, 59 (39%) in Stage C, 94 (50%) in Stage D.

Prostate-specific antigen (PSA) have been determined in all patients.

B-stage patients, after surgical treatment received radiotherapy. Radiation was carried out with x-rays with two juxtaposed fields covering the prostate, total dose 60-70 Gy. Patients with low differentiated tumor and metastases possibility were radiated with two large juxtaposed fields, dose up to 40 Gy, then the fields were reduced so that only the prostate was affected, the dose being increased for 20-30 Gy (total dose 60-70 Gy).

C-stage patients received hormonal therapy (Flutamide) and radiotherapy. D-stage patients received also hormonal therapy, palliative radiation of solitary bone metastases and chemotherapy (4-6 cycles)

**Results:** The observed 5-year survival rates for these series were: 71% for Stage B, 56% for Stage C and 24% for Stage D.

**Conclusion:** We can conclude that due to adequate application of radiation and hormonal therapy the percentage of 5-year survival, particularly with advanced prostate cancer patients, was higher.

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### Ultrasound guided conformal brachytherapy in prostate cancer

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**Purpose:** The management of patients with prostate cancer varies from simple observation to Radical Radiotherapy to Radical Surgery. But the optimal management remains a therapeutic challenge. The indisputable

goal remains to be the optimization of treatment to decrease the treatment related complications.

The choice between surgery and radiation therapy depend on patient satisfaction and quality of life parameters. The results of Radical Radiotherapy have improved over the past decade with advances in methods of treatment delivery with 3-D Conformal Radiotherapy / Interstitial Brachytherapy.

Brachytherapy can be given as a sole radical treatment in early stage or as a boost after External Beam Radiotherapy in later stages. This can be done by using either a permanent I-125 implant or temporary Ir-192 implant using a perineal template. The advantage of temporary Ir-192 implant are that more conformity of the dose can be achieved due to pre-determined fixed geometry of the implant and a post implant modification and optimization can be done by differential loading of sources.

Methods: We have treated eight patients during the period between September 1998 - April 2000. The follow up of the patients ranged from 5 months to 24 months. The age ranged from 54 to 76 years. All the patients had a Biopsy proven prostate adenocarcinoma T1 to T3 tumor and no nodal or distant metastases after a thorough work up. Three patients had Radical Brachytherapy and five patients had Brachytherapy as a boost. The dose delivered with Radical Brachytherapy ranged from 6000 cGy to 7000 cGy. In other patients a brachytherapy boost of 2000 to 2500 cGy was given after external beam radiotherapy, of 4500 cGy to 5000 cGy. Three of the eight patients also received Hormonal treatment.

Interstitial Perineal Implant was done using a perineal template using Ir-192 sources. Needles were placed through the template under the guidance of a per rectal ultrasound probe. This helped in the accurate placement of needles, as there is an online visualization of prostate, rectum and urethra. It also takes into consideration movement of prostate and fixes it. Results: Among the 8 patients, all patients had complete remission clinically and radio logically. At the time of last follow up, 6 patients had normal PSA levels, 8/8 patients are alive. One patient developed nodal metastases after a follow up of 6 months and another patient developed Bone Mets after a follow up of 4 months.

Toxicities were minimal. Two patients had diarrhea & tenesmes; four days following implant & had remission in another 5 days. Three patients had dysurea, increased frequency. None of them had Grade III/IV complications.

#### Conclusions:

In our small study U.S. guided perineal Interstitial Implant using Ir-197 is well tolerated with minimal morbidity and good local control.

## METASTASES

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### The responsiveness of bone metastases in breast cancer patients to radiotherapy with six fractionation schedules

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The aim of this paper was assessment of values of different regimens of radiotherapy fractionation, determining radiologically assessed response, as well as analysis of effect of further evolution of the disease with impact on quality of life and on overall survival in breast cancer patients with bone metastases.

This study was prospective nonrandomised clinical trial performed during the period: 1.1988 - 12.1996, in the Institute for Oncology and Radiology of Serbia (Belgrade) to evaluate the effectiveness of six different radiotherapy schedules for bone metastases local field irradiation. These schedules were: (A) short - 14 Gy/2 fractions, 48 hours interval between them and 16 Gy/4 fractions; (B) median - 18 Gy/6 fractions and 20 Gy/8 fractions; and (C) long ones - 30 Gy/10 fractions and 40 Gy/20 fractions. A total of 386 patients (441 irradiated lesions) with breast cancer and osteolytic bone metastases as a first and sole relapse of the disease, were included in this trial.

Looking at the relation between response rate and subjection to treatment arms A (No=122), B (N=250) and C (No=14) no statistical differences were notable. The probability of five years survival of patients with bone metastases and first and sole relapse was 45.01%, with median overall survival of 31 months. Presence of non-skeleton metastases determines poor prognosis. Response quality to undertake treatment by irradiation is not predictor of overall survival. The patients with favorable finding in irradiated skeleton in the latest registered control had significantly longer survival, than those with finding of evident progression.

It is concluded that short fractionation radiotherapy regimens is as effective as median and long ones in palliation of bone metastases in breast cancer

patients with this form of metastatic disease.

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### Efficacy of percutaneous osteoplasty combined with radiotherapy for painful bone metastasis.

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Purpose: To evaluate the effect of percutaneous osteoplasty (POP) as well as to investigate the efficacy of POP combined with radiotherapy for painful bone metastasis.

Methods: Of 28 patients treated with POP for painful bone metastasis over the past three years, 12 underwent POP only and 16 at the start or end of radiotherapy. The puncture was made under CT fluoroscopic guidance with a bone biopsy needle, specifically in cases of spinal metastasis via the vertebral pedicles. After placement of the needle in the metastatic bone, methyl methacrylate polymer was manually injected under CT fluoroscopic observation. The results of this method in terms of pain relief were evaluated and the efficacy for painful bone metastasis of combining POP with radiotherapy was also investigated.

Results: All procedures were safely and successfully completed. Methyl methacrylate polymer was injected at 1-8ml (average 3.5ml) per single injection. The score on the visual analogue scale for bone pain decreased significantly within one or two days following this procedure for all patients except two who gained pain relief as a result of radiotherapy. Combining radiotherapy with POP produced additive pain relief. Pain relief was obtained with POP, even where radiotherapy had little effect. As a result, complete pain relief was achieved in 25 of 28 patients (89%) by using POP or combination therapy.

Conclusions: POP produced rapid pain relief and an improved quality of life. Furthermore, combining radiotherapy with POP enhanced the pain relief. Percutaneous osteoplasty combined with radiotherapy thus represents an attractive treatment procedure for patients with painful bone metastasis.

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### Results of radiation therapy in skeletal metastases

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This study is aimed to analyse the results of palliative radiation therapy in the patients with skeletal metastases. From June 1993 to September 1995, 132 patients with skeletal metastases were treated with palliative radiation therapy. There were 73 males and 59 females. Majority of the patients were in the age range of 41-60 years (median, 52 years; range 14-80 years). The anatomic sitewise distribution was as follows: spine-86, pelvis-40, rib cage-18, long bones-17 and skull-6 patients. The common primary sites were breast, prostate, lung, myeloma and unknown primary cancers. Doses of radiation ranged from 8 Gy to 40 Gy in different dose fractionation schedules. Single fraction treatment of 8 Gy was the commonest regime (66 patients). The other commonly employed dose fraction regimes were 10 Gy/2F/2 days, 15 Gy/3F/3 days and 20 Gy/5F/5 days depending upon the primary cancer and the expected survival. Twelve patients were lost to follow up and hence 120 patients were evaluable for response to treatment. Ninety four patients (71%) had more than 50% symptomatic response (CR+PR), 20% showed no response or progression of symptoms. Single fraction of 8 Gy provided similar responses as compared to multiple fractionated regimes. Median survival period for cancers of prostate, myeloma, breast and lung was 18, 12, 10 and 5 months respectively. To conclude, radiation therapy is an effective modality for palliation of skeletal metastases in a significant number of cases. Results of single fraction and multiple fraction treatments are almost similar and therefore it is suggested that single fraction of 8 Gy should be preferred in the circumstances where radiotherapy resources are limited and patients have to travel long distances to attend hospital.

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### Avoidance of geographic miss in radiotherapy of the metastatic bone tumors using ct or mri findings in addition to the simple radiography

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Purpose: Radiotherapy is quite useful for the relief of pain associated with