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NICOTINAMIDE COMBINED WITH RADIATION THERAPY IN GLIOBLASTOMA MULTIFORME. Cartei F, Fatigante I, Ducci F, Laddaga M. Radioterapia - Università Pisa - Italy.

The effects of Nicotinamide as a radiosensitizer in animals are well known. In order to extent its use in clinical practice, pharmacokinetic properties and tolerance were studied in seven pts. affected by Glioblastoma and treated with radiation therapy in two fractions per day. Nicotinamide was given orally as two doses of 4g. and 2g. separated by a 6 hours interval. It was well tolerated and had no effect on blood pressure, pulse or body temperature. Pharmacokinetic analysis showed peak plasma concentration above 100 mg/L within 45 min. after ingestion of both doses. This was followed by a biexponential decay of which the terminal T_{1/2} was around 9 h. Tumors were irradiated 1 h. after each drug dose and although it is too early to comment on the tumor response, the drug levels achieved should be sufficient to improve radiation therapy.

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IS THERE A VOLUME EFFECT FOR ACUTE SIDE-EFFECTS FOLLOWING PELVIC RADIOTHERAPY?

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Conformal radiotherapy aims to reduce the amount of normal tissue in the high dose volume and thus lead to a reduction in the incidence and severity of side-effects.

Aim - To examine whether a reduction in the volume of bowel and bladder treated to a high dose during a course of pelvic radiotherapy is associated with a decrease in the incidence and severity of acute radiation induced reactions.

Methods - At the Royal Marsden Hospital there is an ongoing randomised study of conformal pelvic radiotherapy in which dose/volume data and acute toxicity scores have been prospectively analysed. 81 patients with pelvic tumours treated with conventionally fractionated radiotherapy are included in this interim analysis (prostate 74, bladder 7). Doses delivered were 60-64Gy. All patients were seen weekly during treatment. The maximum bowel and bladder side-effects experienced have been recorded using the RTOG acute toxicity scoring system. Full 3D dose calculations were performed and dose/volume histograms were constructed. The volumes of rectum and bladder receiving $\geq 90\%$, 70% and 50% of prescribed target dose have been related to the maximum toxicity score.

Results - The table shows the mean volume of rectum treated to the 50%, 70% and 90% isodoses for patients experiencing different RTOG toxicity scores. There was no correlation observed between volume treated and complication grade. Similar results were observed with bladder side-effects/volume.

Bowel	RTOG toxicity score	No	Mean volume of bowel treated (cc)		
			50%	70%	90% (isodose)
0	24	63	40	32	
1	34	56	44	28	
2	23	53	50	26	

Conclusion - This analysis does not support a dose correlation between acute radiation induced toxicity and the volume of tissue irradiated in the pelvis. Late normal tissue damage is dose limiting and collection of late effect data is underway to determine the volume effect for late damage.

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THE EFFECT OF TREATMENT GAP: THE ISOEFFECT DOSE DEPENDS ON GAP POSITION AND DURATION.

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The analysis of 847 patients with SQCC of supraglottic larynx showed that position of single gap during radiotherapy is an important prognostic factor. The steepness of tumour control curves in relation to gap position and duration was analysed. The estimated TCD₅₀ values for patients with single gap were generally higher than with no gap within the same T-stage. The differences in TCD₅₀s between patients with no gap and with single gap appear to be least when gap occurred in the middle period of treatment (20-29 day) and greatest for late gap (>29 day) suggesting that dose increment required to counteract a gap depends on gap position and duration. The estimated dose increments to balance an one day of a gap were: 0.2-0.4 Gy for middle gaps, 0.6-0.8 Gy for early gaps and 1.2-2.0 Gy for late gaps. These values have not correlated with T-stage.

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Rectal compliance following pelvic radiotherapy; a prospective study. J.H. Meerwaldt, H.W. Luijsterburg, Medisch Spectrum Twente, Enschede.

Following pelvic radiotherapy including the rectum, patients experience increased stool frequency. In a previous study we investigated small bowel function and faecal production. We postulated the hypothesis that the increased stool frequency was due to a reduced rectal compliance (RC). The present study investigated this hypothesis. 20 patients were included, 3 with corpus uteri ca. and 17 with prostatic ca. We used a highly compliant balloon and measured the pressure in relation to the volume injected into the balloon. The RC was calculated. Another parameter was the max. tolerable volume (MV). The measurements were performed prior to radiotherapy and thereafter at six-monthly intervals. The mean RC decreased from 6.2 ml/cmH₂O to resp. 4.8, 3.4 and 3.1 ml/cmH₂O at 6, 12 and 18 months (p=0.002). The mean MV decreased at the same time from 324 ml to 254, 213 and 186 ml. The mean stool frequency increased from 6.8 to 9.4, 12.8 and 11.5 times/day. With increase dose there is a larger decrease in RC. Two patients experienced severe complications, one symptomatic radiation proctitis and one rectal ulcer. They showed a substantial decrease both in RC and MV. In conclusion: Increased stool frequency is linked to reduced Rectal Compliance.

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CONSERVATIVE TREATMENT OF OESOPHAGEAL CANCER. FIRST RESULTS ABOUT 213 PATIENTS TREATED BY CONCOMITANT RADIOTHERAPY (SPLIT COURSE) AND CHEMOTHERAPY

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To decrease toxicity of concomitant radio-chemotherapy, split course radiotherapy was adopted with concomitant chemotherapy for the treatment of 213 patients with oesophageal cancer between January 1987 and December 1992 in our institution.

Characteristics of patients: mean age 63; sex: males 96%; location: middle third 56%; staging (JICC 1978): stages I & II 60%, III & IV 40%.

Characteristics of treatment: Radiotherapy: 2 courses of 5 daily fractionated dose of 3.70 Gy separated by 2 weeks without treatment. Radiation field extended at least 5 cm above and below the tumor. Chemotherapy was delivered at the same time as radiotherapy: Cisplatin (100 mg/m²) or Mitomycin (10 mg/m²) J1 and 5 Fu (1000 mg/m²) in a continuous infusion for the days J2, J3, J4 of each course of radiotherapy. Chemotherapy was continued with 6 cycles for only responder.

Results: Toxicity: gastrointestinal toxicity, the most frequent, never led to discontinue the initial course treatment. Grade III & IV toxicity were hematologic (10 cases) renal (1 case) and neurologic (1 lethal case).

Local response 68% (complete endoscopic response 55%).

Survival: global median survival 15 months (stage I and II: 22 months, stage III and IV: 9 months).

2 years survival 30% (stage I: 80%, stage II: 43%; stage III & IV: 10%).

Conclusions: In this combined modality, the split-course radiotherapy can obtain a benefit in confort treatment with a shorter time of hospital stay and less severe mucosal toxicity than a classical modality of radiotherapy, without leading to a loss of efficiency in local response rate and in survival. The results in survival about the limited lesions suggest strongly that chemotherapy is equal to surgical excision alone.

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STEREOTACTIC RADIOTHERAPY FOR IRREGULAR TARGETS: COMPARISON BETWEEN NON-COPLANAR ARCS AND STATIC NON-COPLANAR CONFORMAL BEAMS

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Stereotactic radiotherapy using a linear accelerator is usually equated with the technique of delivery using multiple non-coplanar arcs which achieve a spherical dose distribution. The majority of intracranial lesions are not spherical. A range of schematised tumour shapes were planned to assess the role of static conformal beams in the treatment of irregular lesions.

A sphere and 2 ellipsoids, ranging from 20 to 50 mm maximum diameter located intracranially were planned using three, four, and six non-coplanar static beams with conformal blocks and were compared to four 120° non-coplanar arcs. Comparison of the plans was made by the relative sparing of normal tissue outside the target volume using 3 dimensional dose-volume distributions. Non-coplanar arcs spared more normal tissue at low isodoses and achieved the best high dose sparing for spherical targets. For the majority of irregular targets 3 and 4 static beams spared more tissue at doses $\geq 50\%$ and $\geq 80\%$ than the arc technique. For all irregular volumes maximum sparing of normal tissue to isodoses $\geq 50\%$ and $\geq 80\%$ of the treatment isodose was obtained with 6 static conformal beams.

We conclude that irregularly shaped tumours suitable for stereotactic radiotherapy with linear accelerator are better treated with conformal static non-coplanar beams rather than with multiple arc technique.