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ORIGINAL ARTICLE

Brachytherapy after laser recanalization *versus* external beam radiotherapy after laser recanalization *versus* laser alone in inoperable oesophagocardial cancer: a controlled pilot study

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Summary

Purpose: *To compare the results of combined laser/radiation therapy with laser treatment alone, and to evaluate the potential benefit of brachytherapy vs. external beam radiotherapy after laser recanalization in patients with dysphagia due to oesophagocardial cancer.*

Patients and methods: *Twenty patients with grade 4 malignant dysphagia caused by oesophagocardial cancer underwent Nd: YAG laser desobstruction up to grade 0-1. Ten of them were referred afterwards for external beam radiotherapy at a dose of 30 Gy for 10 sessions, while the remaining were administered endocavitary afteloading brachytherapy at a dose of 2×7.5 Gy. Twenty preselected patients (to maximally match the above group), who successfully underwent laser re-establishment of the continuity, served as controls to the groups described. Criteria for evaluation were: mean interval to re-stenosis, mean number of additional laser procedures needed, mean survival and Karnofski's performance status (PS). Patients were followed to death. Statistical analysis was carried out with the Student's t-test.*

Results: *It was found that laser plus brachytherapy increased almost 3 times the interval to re-stenosis and decreased almost 2 times the need of additional laser usage in comparison to laser alone. It was also found that laser plus brachytherapy is statistically superior option to laser plus external beam radiotherapy.*

Conclusion: *Laser plus brachytherapy has the potential to become a single modality-single session treatment for the relief of dysphagia in patients with stage IV oesophagocardial cancer.*

Key words: brachytherapy, external beam radiotherapy, Nd: YAG laser, oesophagocardial cancer, palliation

Introduction

Since 1984, Nd: YAG laser treatment of obstructive esophagocardial cancers is considered a standard procedure [1-3]. Despite its benefits, however, the repetitive laser sessions of desobstruction were considered a major nuisance and the major obstacle to an even wider application of the method.

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The pioneering work of Sander et al. [4] to combine laser re-establishment of the continuity with afterloading iridium-192 brachytherapy was a real glimpse of hope. Further on, other researchers have shown that combination of laser re-canalization and brachytherapy is purely beneficial to all kinds of malignant obstructive diseases of the airways and may eventually prolong the survival of patients [5-7]. At the same time, researchers in the U.K. postulated that combination of laser and radiotherapy is potent of significant reduction of the repetitive laser sessions required by the patients [8,9].

This was the scientific environment in the early 1990s, when we started a controlled study on the effectiveness of the following combinations: laser plus definite external beam radiotherapy vs. laser plus brachytherapy in malignant dysphagia caused by stage IV oesophagocardial cancer.

Patients and methods

Twenty consecutive male patients with dysphagia due to stenosis caused by oesophagocardial cancer were submitted either to:

1. Laser desobstruction up to grade 0-1 dysphagia plus definite external beam radiotherapy (DXRT) at a dose of 30 Gy in 10 consecutive working days (10 patients), or:

2. Laser desobstruction up to grade 0-1 dysphagia, plus endocavitary afterloading brachytherapy at a dose of 2×7.5 Gy in 2 sessions, with a time interval of 10 working days between them (10 patients).

Twenty preselected patients (to match best the patients in the groups under study), who had undergone laser desobstruction alone served as controls to the groups under study.

The grade of dysphagia was assessed according to the 4-stepped scale of Krasner and Beard [10].

Laser re-establishment was performed by a CW Nd:YAG laser (MCW 100, Ésculap-MEDITEC, Germany) via a 600 μ light-guide quartz fiber, at $\lambda = 1.064$ μm, as described in the relevant literature.

Definite external beam radiotherapy was performed with standard Betatrone equipment.

Brachytherapy was performed on Microselectron HDR (Netherlands), using afterloading technique on iridium-192. After the initial laser treatment, a tube with an X-ray-positive guide wire was placed in such a manner as to overlap at least 3.0 cm the endoscopically visible tumor border, thus ensuring at least 2 cm healthy tissue beyond the tumor irradiated (Figure 1). The depth of the planning target volume (PTV) depended on the applicator used and the thickness of the tumor bulk. It could be precisely delineated only by means of a sectional imaging (CT or MRI) at the time of application with the applicator positioned.

Then two orthogonal - anterioposterior (AP) and lateral chest x-ray radiographs- were made to assure the applicator was in the proper position (Figure 2). The actual irradiation (15 - 20 min) was then performed (Figure 3).

The patient clinical characteristics of the study groups and the controls are shown on Table 1. The groups were almost identical, with the exception of group III, where the length of stenosis was somewhat longer.

The mean dose and mean duration of the initial laser re-establishment are shown on Table 2. It is clear that no difference in the initial parameters of treatment was recorded.

Criteria for treatment evaluation were the following: mean interval to re-stenosis, mean number of additional laser sessions required to maintain a good passage of food, mean survival and Karnofski's PS.

Patients were followed from the initial treatment until the natural end of the disease.

The cause of death and the status prior to it were certified by a qualified physician on standard legal forms, which were received in the National Cancer Center Hospital some time after death.

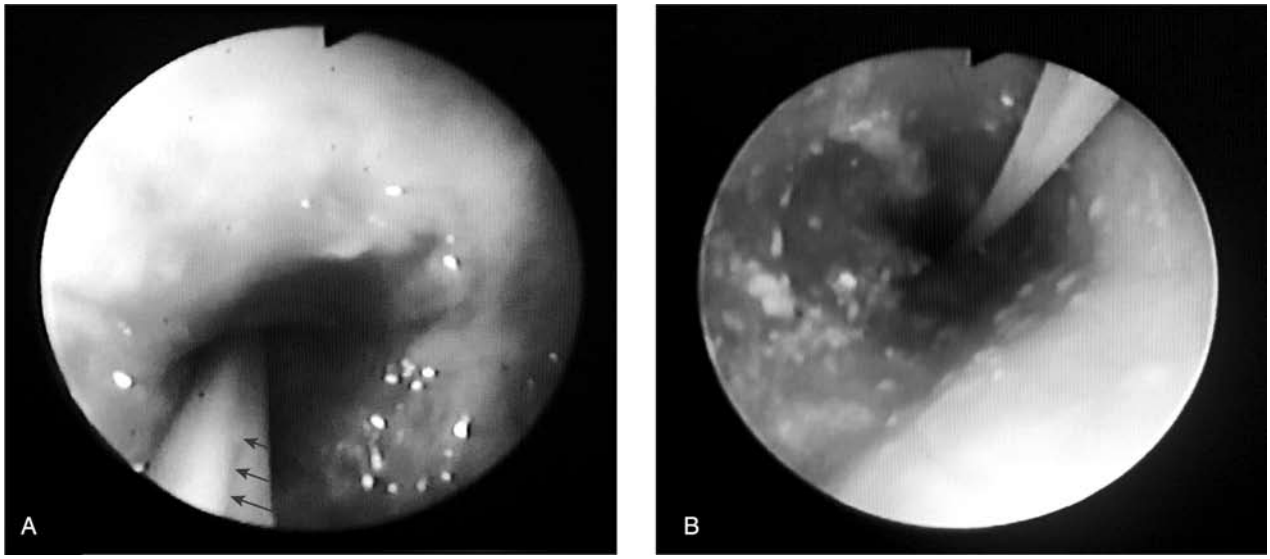

Figure 1. A. The catheter is inserted into the newly re-established continuity. The metal wire guide is visible (arrows). **B.** Withdrawing the endoscope, one should be certain that the catheter is in position and not moved up- or downwards.

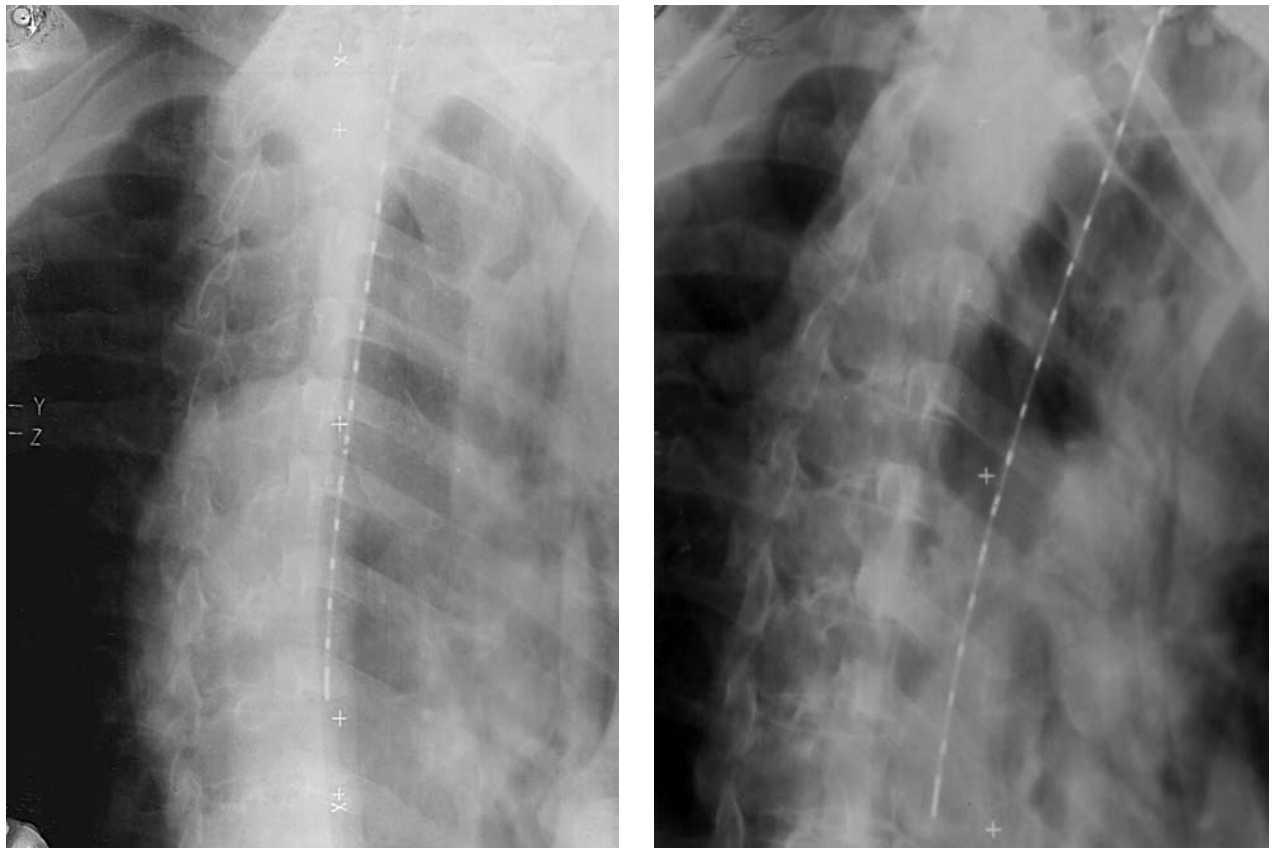

Figure 2. Two orthogonal radiographs (AP - left, and lateral view - right, respectively) are taken immediately at the end of the application.

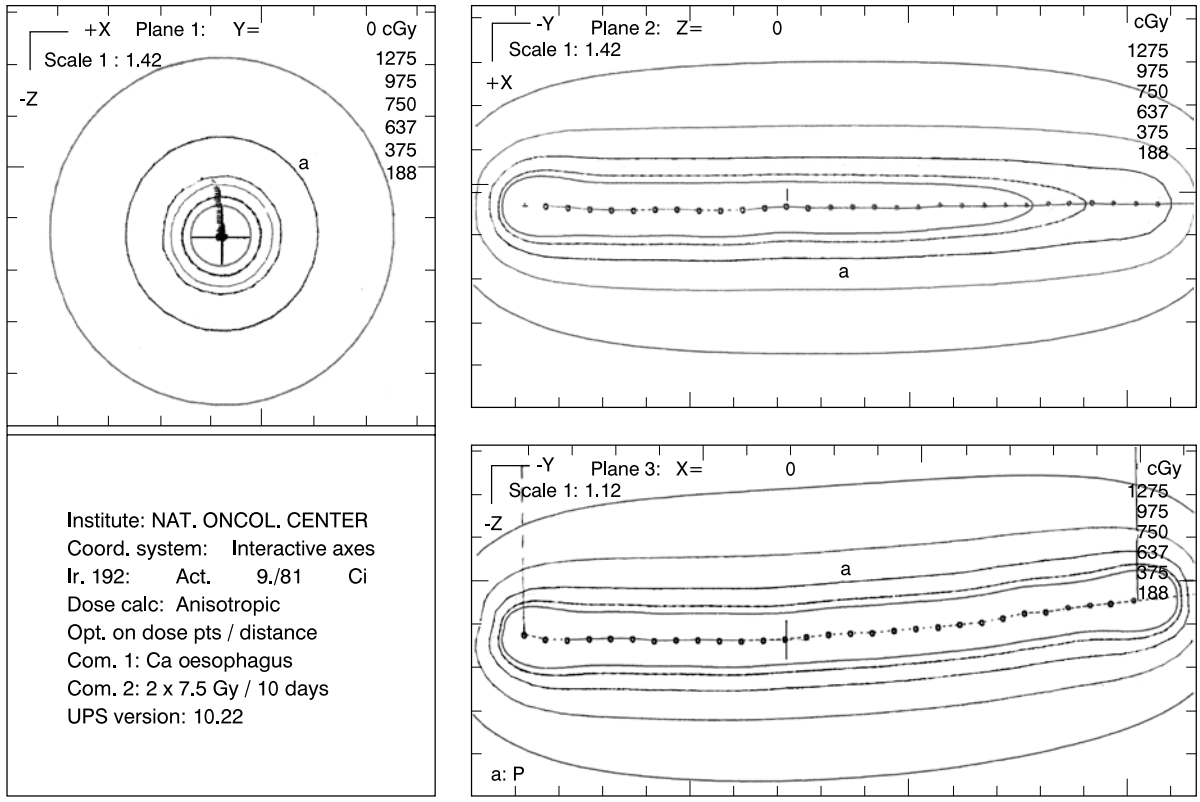

Figure 3. Dose distribution charts: the length of the target volume is 15 cm and the width is 2 cm (1 cm from the source axis).

Table 1. Groups of patients

Group	*Patients, n*	*Age, years (± SD)*	*Histology (adenocarcinoma %)*	*Mean length of stenosis, cm (± SD)*
I§	20	64.4 (11.9)	11	6.7 (2.9)
II†	10	65.3 (12.7)	12	6.5 (3.1)
IIIp	10	62.2 (15.9)	10	10.3 (4.2)
		p = 1.0	p = 1.0	p < 0.05*

SD: standard deviation, §: laser alone, †: laser plus DXRT, p: laser plus brachytherapy; *III compared to either group II or I

Table 2. Mean dose and mean duration of the initial laser re-establishment

Group	*Mean dose (J)*	*p-value*	*Mean duration (days)*	*p-value*
I	11792.0		4.3	
II	11908.0	NS	4.1	NS
III	14632.0	NS	4.7	NS

For patient grouping see footnote of Table 1
NS: non significant

The study started in 1994 and was closed in 2004, when the last record of the last patient was received in the National Cancer Center Hospital.

Statistical analysis was made with Student's *t-test*. Statistical significance was accepted at $p < 0.05$.

Results

Results on the mean interval to re-stenosis and mean number of additional laser sessions required to maintain a good food passage are presented on Table 3.

It is clear that laser plus brachytherapy has the potential to significantly reduce the need of additional laser usage compared with both laser plus DXRT and laser alone; in addition the time to re-obstruction was significantly longer compared to laser plus DXRT and almost 2.5 times longer compared to laser alone.

None of the methods showed prolongation of survival of either the patients under study or the controls. Some deviation of the results concerning Karnofski's PS occurred in the group with laser plus brachytherapy, indicating a poorer quality of life, not reaching, however, statistical significance (Table 4). The longer length of stenosis in this very group might be the cause of this observation.

Discussion

It was once postulated that a single dose of high dose rate (HDR) brachytherapy may have a beneficial effect on dysphagia in malignant obstruction of the passage [11-13]. It was also demonstrated in multiple randomized trials that brachytherapy may be superior to metal stenting in the treatment of malignant dysphagia [14,15].

To the best of our knowledge, no one has ever tried to study how malignant tissue reacts after laser treatment with either percutaneous (external beam)

Table 4. Mean survival and Karnofski's PS

Group	*Survival after treatment (mean, months)*	*p-value*	*Karnofski's PS*	*p-value*
I	6.2		70	
II	6.5	NS	72	NS
III	6.4	NS	68	NS

For patient grouping see footnote of Table 1
NS: non significant

Table 3. Mean interval to re-stenosis and mean number of additional laser procedures required

Group	*Mean interval to re-stenosis (days)*	*p-value*	*Mean number of additional laser sessions required*	*p-value*
I	97.3		2.7	
II	143.6	p <0.001	1.5	p <0.001
III	207.4	p <0.0001	0.6	p <0.0001, p <0.005*

For patient grouping see footnote of Table 1
*comparison of groups II and III

or intracavitary afterloading brachytherapy, to ensure the best quality of life for incurable patients with severe dysphagia due to stage IV oesophagocardial cancer.

Our study is maybe the first to compare laser alone, laser plus DXRT and laser plus brachytherapy. Its interest does not lie with its uniqueness but rather with the results obtained.

In our series (though not large, as it was designed as a pilot study), patients with laser plus brachytherapy needed almost 5 times less additional laser sessions to maintain their passage compared to patients with laser alone, and almost 2.5 times less sessions compared with laser plus DXRT. At the same time the mean interval to re-stenosis was almost 2.5 times longer compared to laser alone and almost 2 times longer compared to laser and DXRT. It is worthwhile mentioning that none of the methods had the potential to prolong survival, which was rather unexpected. Slightly disturbing was the relatively lower (but nonsignificant) quality of life in the group with laser plus brachytherapy. We can certainly speculate on the length of stenosis, of the variety of factors involved in the assessment of PS etc, but none-the-less we should never be able to statistically conclude what really caused such an impact on this group. Future larger scale randomized studies may possibly give an answer to such a question.

Studies of other researchers are in agreement with our results with respect to the combination of laser plus brachytherapy [16-18]. This is, however, a partial confirmation since no one was inclined to compare laser plus DXRT vs. laser plus brachytherapy.

Maybe similar studies will appear in the future and comparisons could be made possible. For the time being the present study has no analog in the literature and that's why it's so difficult to interpret the results taken and their deviations.

Conclusions

1. Laser plus DXRT significantly reduces the need for additional laser procedures in stage IV oesophagocardial cancer.

2. Laser plus DXRT prolongs twice the interval to re-stenosis after initial laser treatment in stage IV oesophagocardial cancer.

3. Laser plus HDR brachytherapy increases almost 3 times the interval to re-stenosis in comparison with laser alone, and almost twice after laser plus DXRT.

4. Laser plus HDR brachytherapy decreases almost 4 times the need for additional laser sessions in stage IV oesophagocardial cancer, and almost 2.5 times compared to laser plus DXRT.

5. None of the methods prolongs patient survival.

6. None of the methods is superior in achieving better PS.

7. Laser plus HDR brachytherapy has the potential of becoming a single modality-single session method to ensure the best quality of life in patients with stage IV oesophagocardial cancer.

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