

# Efficacy of early postoperative radiotherapy for nonfunctioning null cell or silent pituitary macroadenomas

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## INTRODUCTION

The high voltage radiotherapy (RT) after surgery for nonfunctioning pituitary macro adenomas (NFMA) is still controversial, subjected to rapid technical and medical progress.

## AIM

To appreciate the best period of time for RT in patients with pituitary macro adenomas with residual tumor after surgery.

## SUBJECTS AND METHODS

We studied 97 patients with residual NFMA to identify factors affecting tumor control such as the time of RT and tumor immunopathology. Partial pituitary surgery was performed either by trans frontal (35 patients) or transsphenoidal (62 patients) approach. High voltage RT (mean total dose 50.5 Gy) was given to 41/97 patients. Twenty out of 41 patients had RT within the first year after surgery (Group A) and 21/41 had RT after 1 year (Group B). Fifty six out of 97 patients with surgery, without RT, represent the control group (Group C) (Fig.1). The increase of the postoperative remnant was defined as a minimum 25% increase of any diameter (either transversal or vertical) by serial imaging studies. The immunoperoxidase analysis (avidin biotine technique) for the anterior pituitary hormones and the final immunopathological classification of the NFMA revealed: 44 null cell adenomas (a) (immunostaining was negative for all hormones), 23 gonadotropinomas (b) (positive immunostaining for LH $\beta$  and FSH $\beta$ ) and 30 plurihormonal (immunostaining positive for more pituitary hormones different from gonadotropins) or unihormonal silent adenomas (c) (immunostaining positive for ACTH, GH or PRL), (Table1).

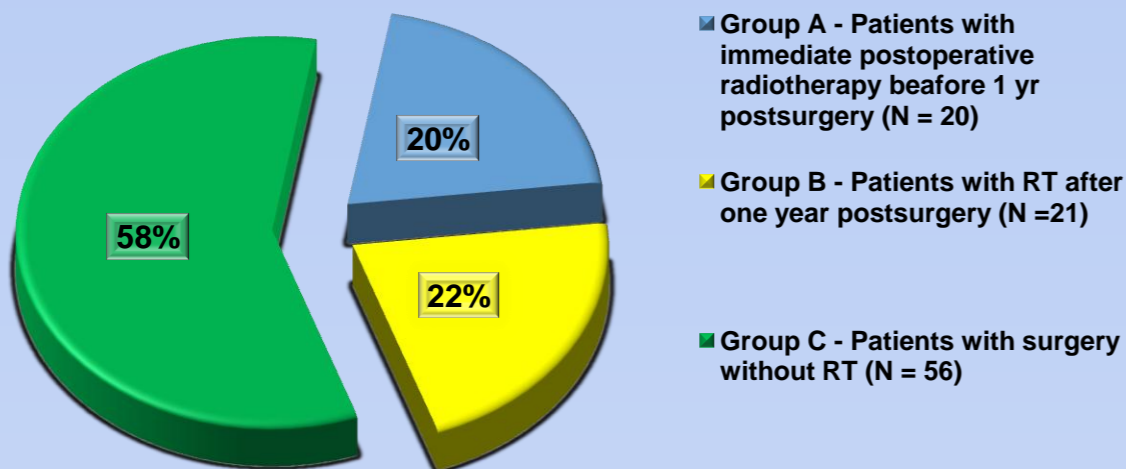


Figure 1. Types of treatment.

Table 1. General characteristics of patients

	Patients with radiotherapy after surgery (N = 41)		Control Group Group C (N = 56) Patients after surgery, without RT
	Group A (N = 20) RT up to 1yr	Group B (N = 21) RT after 1yr	
Mean age of diagnostic (yrs)	44.5 ± 11.64	47 ± 11.62	50 ± 12.92
Sex ratio (M/F) n	10/10	18/3	28/28
Mean size (range) postoperative remnant (cm)	2.72 (0.90-4.70)*	1.94 (0.66 – 4.50)*	1.63 (0.50 – 5.50)*
Patients with remnant greater 2 cm in size (n,%)	15/20 (75%)*	10/21 (48%)	17/56 (30%)*
Patients with supra sellar remnant (n,%)	15/20 (75%)*	14/21 (67%)*	21/56 (37%)*
Mean (range) time of RT after surgery (mo)	6 (2-12)	24 (14-89)	-
Cavernous sinus invasion (n,%)	13/20 (65%)*	7/21 (33%)	21/56 (37%)*
Visual field deficits	14/20 (70%)	18/21 (86%)	41/56 (73%)
IHC a/b/c	7/3/10	12/4/5	25/16/15

\*p<0.05, Group A vs Group C and Group B vs Group C

## RESULTS

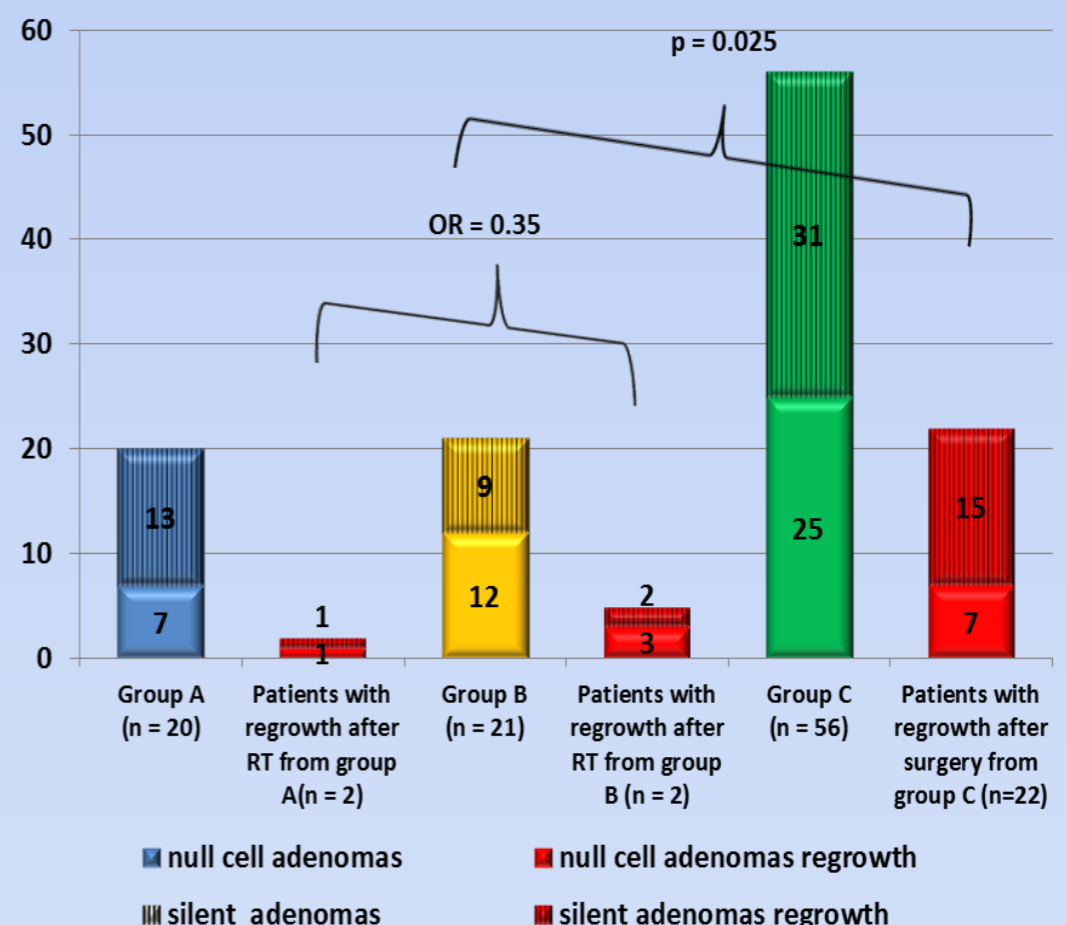
Table 2. The rate of the residual tumor regrowth in relation to the high voltage radiotherapy (RT)

Total number of patients (n = 97)		No. of patients with regrowth at 5 years according to postoperative RT			No. of regrowth after surgery without RT according to immunohistochemistry		No. of regrowth after RT according to immunohistochemistry	
		RT + (< 1yr)	RT + (>1yr)	No RT	Null cell	Silent hormone	Null cell	Silent hormone
Null cell adenoma	Silent hormone adenoma							
44 (45%)	53 (55%)	2 (2%)	5 (2%)	22* (39%)	7 (16%)	15* (28%)	4 (9%)	3 (6%)

\*p < 0.05 vs patients with RT

Patients without RT (control group C) have a significant higher regrowth rate of residual tumor versus patients with RT (p = 0.025), at 5 years. Only 2/20 patients with immediate RT (group A) have regrowth at 5 years and 5/21 patients from group B, see Table 2, Fig.2. The chance for the remnant regrowth is decreased in group A vs group B (OR = 0.35). It is important to emphasize that patients from group A vs patients from group control, without RT, have had more tumors with cavernous sinus invasion (p = 0.038), with high postoperative remnant (p = 0.001) or with size more than 2 cm (p = 0.001) and with residual mass outside the sella (p = 0.003). Patients from group B vs control, group C, showed also statistically significant higher postoperative remnant (p=0.047) and residual mass with suprasellar extension (p=0.023), (Table 1).

Figure 2. The regrowth up to 5 years of the postoperative remnant of the null cell and silent uni/plurihormone pituitary macro adenomas



In the control group C, without RT, the patients with silent hormone adenomas have a regrowth rate more frequently than patients with null cell adenomas (p=0.060, CI 90%), (Table 2).

In the groups A and B, we observed by contrast that postoperative RT is associated with lower risk of residual tumor regrowth for these type of tumors expressing hormones vs null cell adenomas (OR = 0.16) (Fig 2).

## CONCLUSIONS

It is tempting to suggest as an optimal time for radiotherapy is the first year post partial surgery of nonfunctioning pituitary macro adenomas. Special attention should be given for uni/plurihormonal silent adenomas (as shown by immunohistochemistry).