

Supplementary Table 2: Details of included studies: growth velocity

Study (year) - Design	Population (n)	Histology	Sex M/F	Age mean (range)	Imaging modality	Method of growth measurement	Time between serial imaging	Mean follow-up in years (range)	Growth pattern	Tumour growth velocity
Ayalon-Dangur (2023) - Retrospective cohort	Treatment-naïve macroNFAs (49)	n.a.	14/19 ^o	68±12 [^]	MRI	Maximal diameter increase	n.r.	5 (1-22) ^o	Increase: 16 (33%) Stable: 23 (47%) Decrease: 10 (20%)	Mean 0.46 mm/year (range 0-6) ^o
Dekkers (2007) - Retrospective cohort	Treatment-naïve macroNFAs (28)	n.a.	15/13	55±3 [^]	0.5 to 1.5 tesla MRI with in-plane spatial resolution of 0.74 x 0.37 mm	Volume of a rotating ellipsoid: $\pi/6(V \times AP \times T)$	Repeat MRI performed ≤1 year after initial diagnosis, if no growth observed; subsequent MRI every second year	7.1±1.1 [^]	Increase: 14 (50%) Stable: 6 (21%) Decrease: 8 (29%)	Mean 0.6 mm/year or 236 mm ³ /year in 14 patients with tumor growth
Hsu (2010) - Retrospective cohort	Surgically treated PAs (160)	Gonadotroph (65), null cell (16), prolactinoma (24), somatotroph (3), corticotroph (5), plurihormonal (47)	84/76	Median 46 (14-83)	1.5 tesla MRI including T1-weighted coronal view of pituitary fossa with same scanning positioning in pre- and post-gadolinium-based contrast medium administration with 3-mm slice thickness/0-mm gap	TVDT = interval x $\log_2(2)/\log_2(V_2/V_1)$	≥1 month	2.4 (0.2-9)	Increase: 54 (34%) Stable/decrease: 106 (66%)	Postoperative TVDT mean 78.7±148.3 months, median 34.6 months [□] in 54 patients with tumor growth - functioning tumours median 33.7 months - clinically nonfunctioning tumours median 35.4 months
Hwang (2019) - Retrospective cohort	Treatment-naïve PAs (59)	n.a.	28/31	64.4 (23-83)	MRI including gadolinium-enhanced T1-weighted coronal view with 2-mm slice thickness	Tracing contour of tumor area on each MRI slice, then multiplying the sum of the areas by slice thickness	≥1 year	3.9 (1-11.3)	Increase: 16 (27%) Stable: 43 (73%) overleg	Mean 340±680 mm ³ /year
Monsalves (2014) -	Surgically treated macroPAs (153)	Gonadotroph (63), null cell (24), prolactinoma	71/82	53 (25-87)	MRI with dedicated sella/pituitary protocol, including gadolinium-	TVDT = interval x $\log_2(2)/\log_2(V_2/V_1)$	≥3 months	n.r., but every subject had ≥ 1.3	Postoperative residual volume in 53 of 100 patients:	Preoperative TVDT mean 38.2±29 months

Retrospective cohort		(10), somatotroph (16), corticotroph (26, of which 5 silent), plurihormonal (13), thyrotroph (1)			enhanced T1-weighted coronal and saggital views for preoperative scans, and gadolinium-enhanced T2-weighted coronal and saggital views for postoperative scans			years follow-up	Increase: 23 (43%) Stable/decrease: 30 (57%)	- functioning tumours 24.9±18.8 - clinically nonfunctioning tumours 44.5±30.9 - gonadotroph 36.6±22.3 - null cell 52.6±41.2 - prolactinoma 40.7±40.8 - somatotroph 29.8±20.4 - corticotroph 73.8±69.9 - plurihormonal 31.4±16.7 Postoperative TVDT of 23 residual PA's showing growth mean 38.8±20.5 months - functioning tumours 28.6±15.4 - clinically nonfunctioning tumours 42.4±21.2
Øystese (2017) - Retrospective cohort	Surgically treated macroNFAs (52)	'pituitary adenomas'	31/21	Median 56.5 (IQR 48.0-63.0)	MRI including gadolinium-enhanced T1-weighted coronal view with 3-mm slice thickness in the majority	Tracing contour of tumor area on each MRI slice, then multiplying the sum of the areas by slice thickness	n.r.	Median 8.3 (IQR 6.7-9.5)	Increase: 39 (75%) Stable/decrease: 13 (25%)	TVDT median 27.6 months (IQR 18.6-42.9)
Panet-Raymond (2019) - Retrospective cohort	MacroNFAs with residual tumor after surgery (31)	n.r.	19/12	Median 55 (33-77)	MRI including gadolinium-enhanced T1-weighted coronal and axial views with slice thickness ranging from 1 – 5 mm	'tumors were contoured on each imaging slice and volumes were determined'	Initial follow-up images obtained median 8.9 months (range 1-26) post-surgery	Median 4.4 (1.5-7.3)	N.r., but volumetric growth was detected in 95% of 81 postoperative MRI's	Median 446 mm ³ /year (range 11-21900)
Pieterse (2016) - Retrospective cohort	MacroNFAs (13): conservatively managed (7),	n.r.	10/13	49.5 (25-69)	1.5 tesla MRI including gadolinium-enhanced coronal	Tracing contour of tumor area on each MRI slice, then multiplying the sum	n.r.	2.9 (1.1 – 5.8)	Increase: 13 (100%)	Mean 1861 mm ³ /year (range 50-4980) in conservatively

	residual tumor after TSS (6)				and sagittal views with slice thickness ranging from 2 – 5 mm	of the areas by slice thickness				managed tumours, mean 3713 mm ³ /year (range 20-15100) in surgically treated tumours
Ratnasingam (2017) - Retrospective cohort	Surgically treated NFAs (108), of which 24 required secondary therapy	61 specimens available: null (34), plurihormonal (13), positive stain for prolactin (5), LH (3), FSH (2), ACTH (2), TSH (2)	58/50	54.7±3.1 ^{^o} in 24 patients requiring secondary therapy, 52.5±1.7 ^{^o} in 84 patients not requiring secondary therapy ^o	MRI with dedicated pituitary protocol including standardized T2-weighted axial and T1-weighted coronal and sagittal high-resolution spin echo sequence of at most 3 mm thickness	Volume of a rotating ellipsoid: $\pi/6(V \times AP \times T)$	Median 1.6 years (0.4-3.9)	Median 5.7 (1.2-15.1)	Postoperative residual volume in 66 of 108 patients: Increase: 48 (73%) Stable/decrease: 18 (27%)	311 mm ³ /year ^o (range 72-2315) in 24 patients requiring secondary therapy, 23 mm ³ /year ^o (range 15-628) in 84 patients not requiring secondary therapy
Sam (2015) - Retrospective cohort	Conservatively managed NFAs (66): macroadenoma (47), microadenoma (19)	8 specimens available of 9 patients eventually operated on due to visual field deficits: gonadotroph adenoma (6), acidophilic stem cell adenoma (1), clinically silent somatotroph adenoma (1)	28/38	Median 41 [^]	MRI including dedicated high-resolution sagittal and coronal views of the pituitary fossa	Increase in maximal tumour dimension	Every 6-12 months	4.3 (1-14.7)	Increase: 38 (58%) Stable: 6 (9%) Decrease: 22 (33%)	Median 0.8 mm/year (range 0.1 – 7.7)
Tanaka (2003) - Retrospective cohort	Surgically treated macroNFAs with postoperative residu (40)	'typical chromophobic pituitary adenomas with sinusoidal, papillary, or diffuse cellular patterns, with no findings suggesting malignancy'	24/16	53.5 (13-76)	MRI including gadolinium-enhanced T1-weighted coronal views with slice thickness ranging from 2 – 5 mm	Tracing contour of tumor area on each MRI slice, then multiplying the sum of the areas by slice thickness	n.r.	4.4 (0.3-11.8)	Increase: 38 (95%) Decrease: 2 (5%)	TVDT mean 61.2 months (range 16.9-179.3) in 38 NFA's with regrowth after surgery
NFA non-functioning adenoma										

PA pituitary adenoma

TVDT tumour volume doubling time

TSS transsphenoidal surgery

n.a. not applicable

◇ for 33 patients observed without surgery or intervention throughout the follow-up period

^ no range reported

* results n.s. for treatment-naïve or residual tumors

□ difference between mean and median due to skewness 4.09 to the right and presence of a few extremely slow growing cases

○ authors could not be reached to clarify if it concerns mean or median