

# Evaluation of MRI T2-signal intensities of GH-secreting pituitary macroadenoma in treatment-naïve acromegalic patients receiving primary treatment with lanreotide Autogel 120 mg

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## Introduction and objectives

- Acromegaly is a chronic condition characterized by excess growth hormone (GH) secretion, which is caused, in the majority of cases, by a pituitary adenoma.<sup>1</sup> Long-acting somatostatin analogues (SSAs) are well established treatments for acromegaly after unsuccessful surgery, and are also used as first line treatment if surgery is refused, contra-indicated or unlikely to be successful.<sup>2</sup>
- In a previous study, the hypointense T2-signal of GH-secreting pituitary adenomas on magnetic resonance imaging (MRI), which reflects various tissue properties, predicted the biochemical outcome of first-line SSA therapy.<sup>3</sup>
  - However, the definition of T2 hypointensity of GH-secreting adenomas varies between studies. We hypothesize that different definitions of T2 hypo-, iso- and hyperintensities lead to differences in perceived distributions of GH-secreting adenomas, and therefore to differences in reported outcomes after SSA treatment.
- Here, we investigate three methods for evaluating the T2-signal intensity of pituitary macroadenoma, and the extent to which they predict the response to SSA treatment, using additional post hoc analysis of data from the PRIMARYS study (EudraCT2007-000155-34; NCT00690898).

## Methods

- PRIMARYS was an open-label study in which 90 patients with acromegaly received primary medical treatment with the long-acting SSA, lanreotide Autogel (Depot in the USA) at a fixed dose of 120 mg every 4 weeks for 1 year. The study was conducted to evaluate the tumour volume reduction in patients with macroadenomas (diameter  $\geq 10$  mm) via centralized MRI readings. Patients were eligible for inclusion if they were treatment-naïve and had no visual field defects.
- In the current analysis, each MRI was read by a single neuroradiologist to determine T2-signal intensity, using one qualitative method based on a visual assessment (as per daily routine practice) and two quantitative methods, the Heck method<sup>3</sup> and a method using the signal intensity ratio of the adenoma under the grey matter (**Figure 1**).
  - For each method, intensities were rated as hypointense, isointense or hyperintense, as defined in **Figure 1**.
  - The reader was blinded to the identity of the subject and the status of hormonal control and tumour response.
- For each of the three methods, signal intensities at baseline were summarized in the overall population and according to hormonal control and tumour response (endpoints of the PRIMARYS study<sup>4</sup>).
  - Hormonal control was defined as GH levels  $\leq 2.5$  ng/mL and normalized insulin-like growth factor-1 (IGF-1).
  - Tumour response was defined as a reduction in tumour volume  $\geq 20\%$  between baseline and the patient's last visit during the study.
- Multivariate analyses were conducted to evaluate whether, after controlling for other baseline characteristics, baseline T2-signal intensities were associated with the change in GH and IGF-1, hormonal control and tumour response at last study visit available (LVA).

**Figure 1.** Methods used to assess and classify T2-signal intensities of macroadenomas in patients with acromegaly

Visual assessment method	Signal intensity ratio method	Heck method
Compare adenoma T2 signal/cerebral grey matter	Ratio (SR) adenoma T2 signal/signal grey matter	Compare adenoma T2 signal/signal grey matter AND white matter
<b>Hyperintense</b> Adenoma T2 signal > grey matter	<b>Hyperintense</b> SR $\geq 1.2$	<b>Hyperintense</b> Adenoma T2 signal > grey matter
<b>Isointense</b> Adenoma T2 signal = grey matter	<b>Isointense</b> 0.8 < SR < 1.2	<b>Isointense</b> Adenoma T2 signal between grey and white matter
<b>Hypointense</b> Adenoma T2 signal < grey matter	<b>Hypointense</b> SR $\leq 0.8$	<b>Hypointense</b> Adenoma T2 signal < white matter

SR, signal ratio

## Results

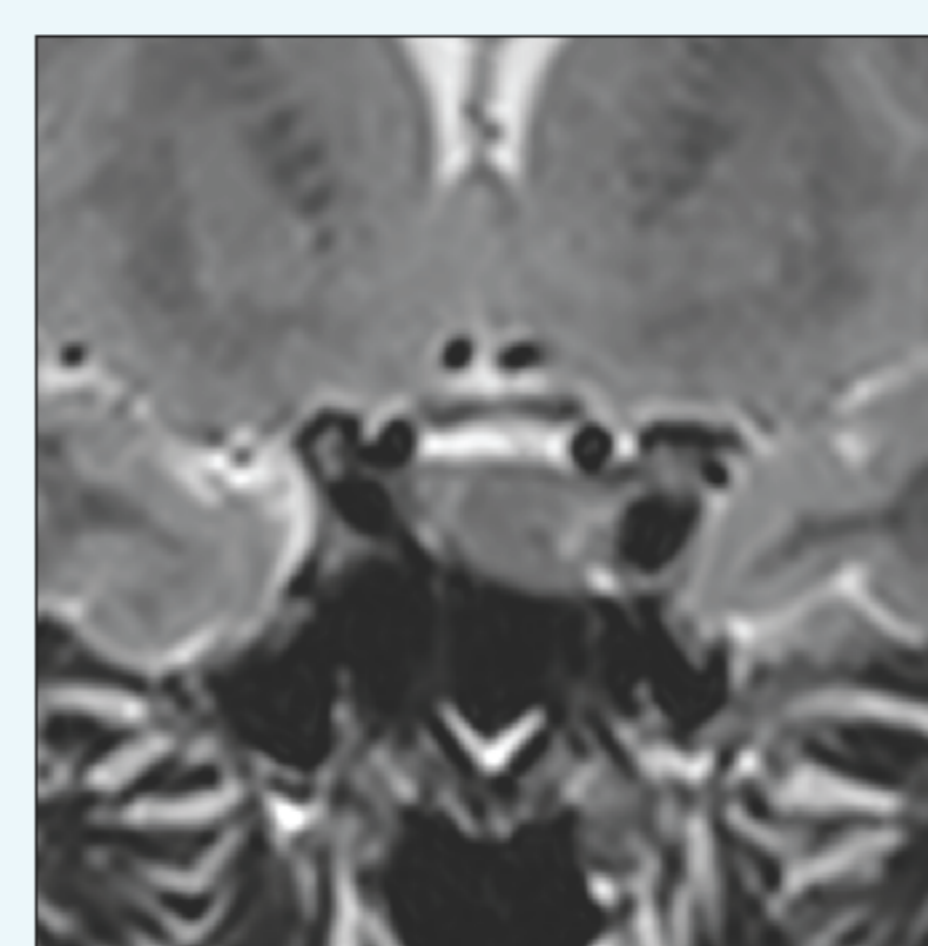
- Baseline T2 signal intensity data were available for 85 patients, of whom 30 achieved hormonal control and 53 achieved tumour response at LVA.
- Overall, more adenomas were classified as hypointense using the visual assessment method (59%) than using either of the quantitative methods (signal-ratio method, 36%; Heck method, 20%) (**Table 1**).
  - Figure 2** shows an MRI scan of a patient classified as hypointense using both the visual assessment and the signal-ratio methods, but isointense using the Heck method.
- Patients achieving hormonal control or tumour response were more often classified as hypointense according to the visual assessment method than with the quantitative methods (**Figure 3** and **Figure 4**).
- As targeted adenomas appear to be hypointense on T2-weighted images, we arbitrarily selected the visual assessment method, which identified most hypointense adenomas, for further analyses.
- Baseline tumour volumes were lower in the hypointense group than in the hyperintense and isointense groups: median (95% CI) volumes were 1158 (959; 1810) mm<sup>3</sup> vs. 4767 (1872; 22 725) mm<sup>3</sup> and 2017 (1387; 4066) mm<sup>3</sup>, respectively.
- There was an additional reduction in GH levels of 4  $\mu$ g/L between baseline and LVA for those with hypointense versus isointense tumours ( $p < 0.0001$ , F-test).
- Similarly, there was an additional reduction in IGF-1 levels (of 65 ng/mL) between baseline and LVA for those with hypointense versus isointense tumours ( $p = 0.0026$ , F-test).
- No association between the T2-signal intensity and hormonal control was identified. However, the odds of obtaining a tumour response were 6.2 times higher for hypointense versus isointense adenomas ( $p = 0.0185$ , Wald test).

**Table 1.** Proportions of patients classified as hypointense, isointense and hyperintense according to T2-signal intensities

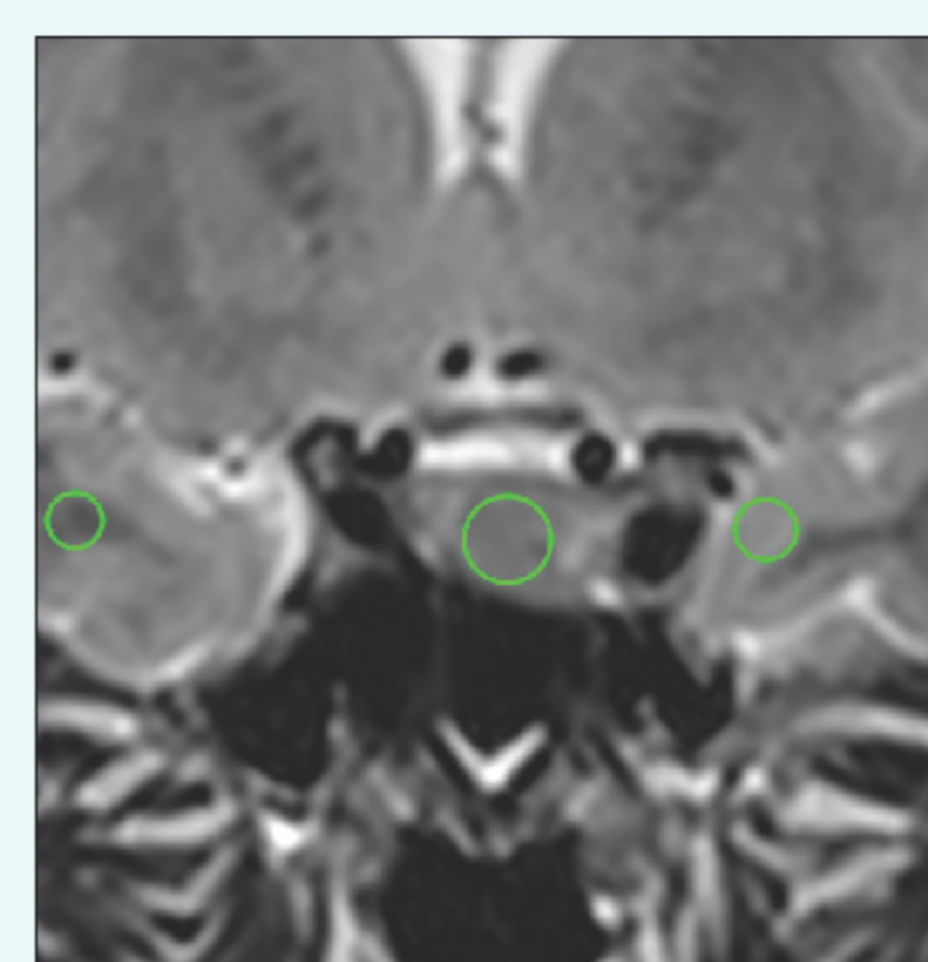
	Visual assessment	Signal-ratio method	Heck method
Hypointense, n (%)	50 (59)	31 (36)	17 (20)
Isointense, n (%)	31 (36)	44 (52)	40 (47)
Hyperintense, n (%)	4 (5)	10 (12)	28 (33)

**Figure 2.** Illustrative example of a GH-secreting pituitary macroadenoma at baseline on MRI (coronal T2-weighted sequence)

(a) Qualitative (visual) analysis

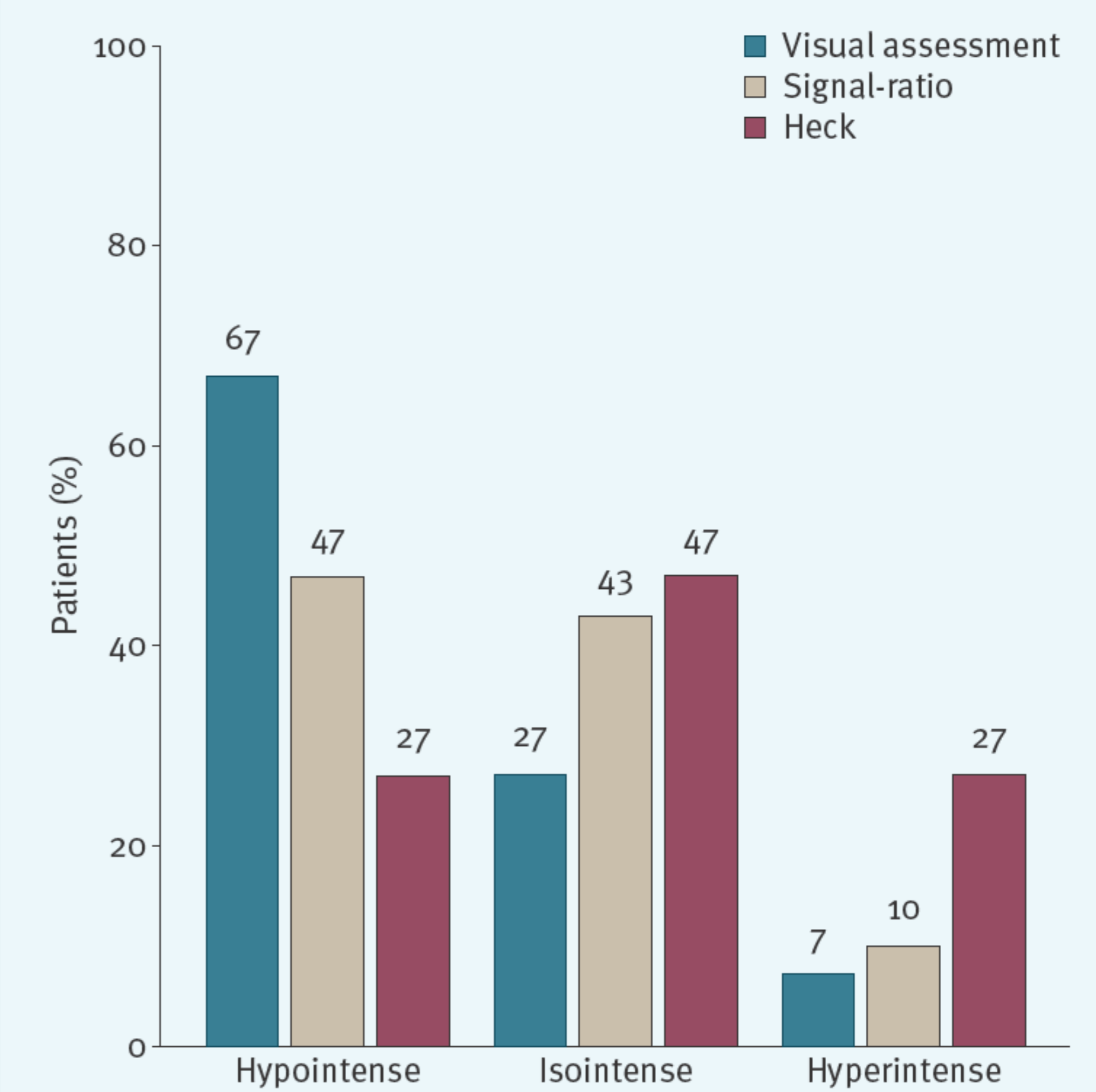


(b) Quantitative analysis

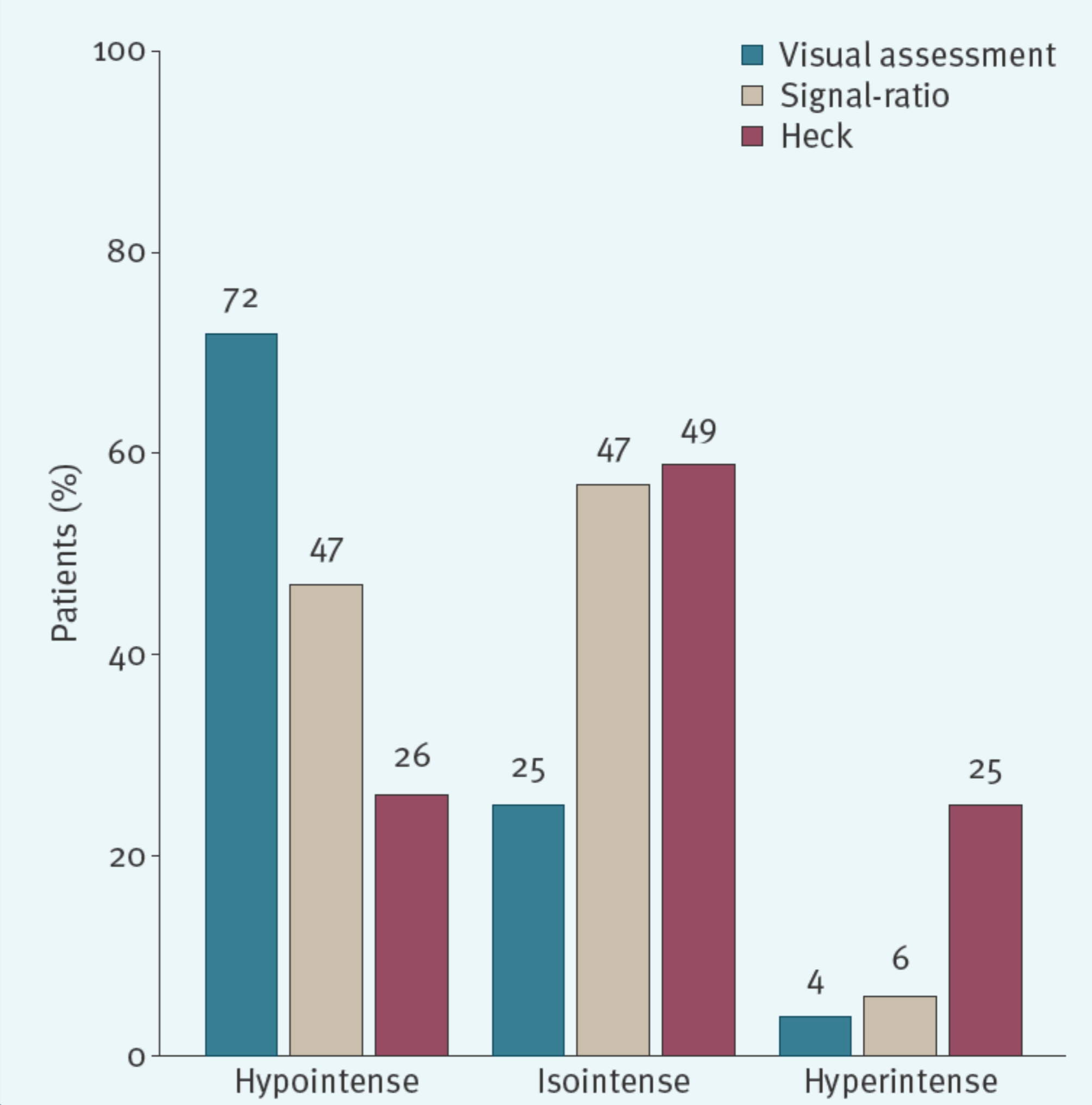


a) On qualitative analysis the adenoma is hypointense (vs. grey matter).  
b) Regions of interest for quantitative analysis (left to right): white matter (290), adenoma (349), grey matter (451). Signal-ratio method, hypointense, because ratio adenoma/grey matter =  $349/451 = 0.77$ ; Heck method, isointense, because white matter (290) < adenoma (349) < grey matter (451).

**Figure 3.** Hormonal control according to baseline MRI T2 signal intensity using visual assessment, signal ratio and Heck methods



**Figure 4.** Tumour response according to baseline MRI T2-signal intensity using visual assessment, signal ratio and Heck methods



## Conclusions

- These results suggest that clinical visual assessment is preferable for the identification of T2-hypointense, GH-secreting macroadenoma in treatment-naïve patients with acromegaly.
- There was a trend towards smaller tumour volumes at baseline in the hypointense group.
- Patients with hypointense lesions have a greater reduction in GH and IGF-1 values compared with those with isointense lesions following primary SSA treatment. In addition, the odds of tumour response are higher.

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### References

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