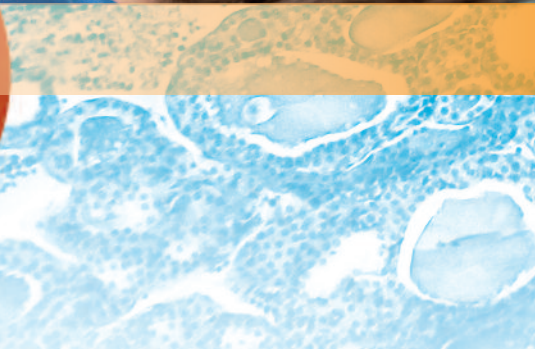




Thermo Scientific B-R-A-H-M-S TRAK human
Immunodiagnostic Assays



The gold standard

in Graves' disease diagnosis

Is it really Graves' disease? • Will my patient relapse? •
Which course of Graves' ophthalmopathy to be expected?

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Diagnostic dilemma

In most countries specific treatments are applied for Graves' disease and toxic multinodular goiter or disseminated autonomy. Making an accurate diagnosis is difficult, even for skilled clinicians and despite using a broad diagnostic spectrum.¹

Laboratory diagnostic approach

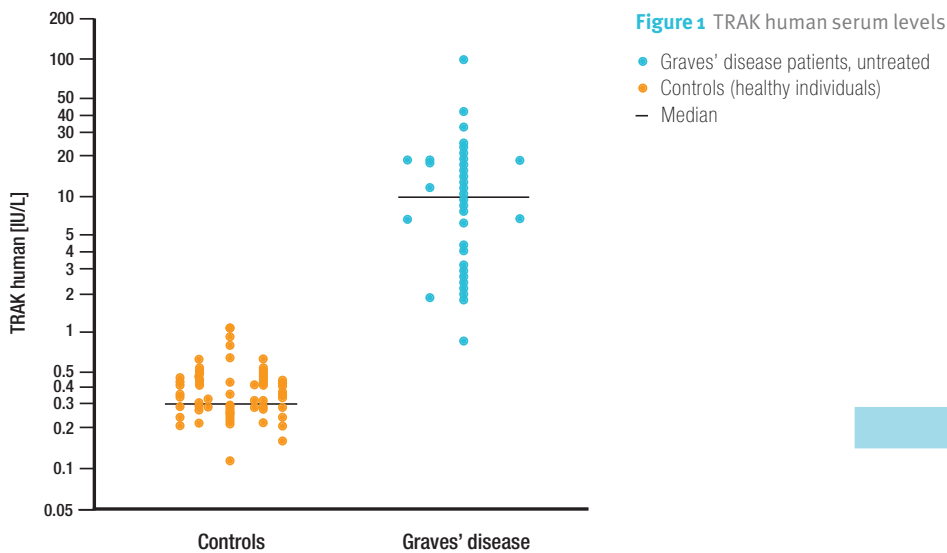
The availability of commercial assays using TSH receptors from porcine thyroid made it possible for the first time to routinely measure TSH receptor auto-antibodies (TRAb).² With the introduction of the highly sensitive Thermo Scientific™ B·R·A·H·M·S™ TRAK human assay in 1999 using immobilized recombinant human TSH receptors a definite improvement for differential diagnosis of Graves' disease was achieved.³





Facts

This was shown by numerous published studies where nearly 2000 Graves' disease patients and controls were included.^{1,3,4-13} The excellent results – sensitivity >98%, specificity almost 100% – in the group of untreated Graves' disease (n=855)^{3,4,6-12} were confirmed by two further thyroid centers^{1,5} (see Fig. 1).



Case report from practice

52 year old woman, nervousness, no weight-loss, non-smoker, no eye-signs, pulse rate 80/min., thyroid clinically inconspicuous/slightly increased (29 mL), Tc scan inhomogeneous, uptake 10%, TSH <0.01 mIU/L

TRAK human 3 IU/L ▶ Graves' disease ▶ antithyroid drug therapy

Relapse or remission?

Clinical course after antithyroid drug therapy

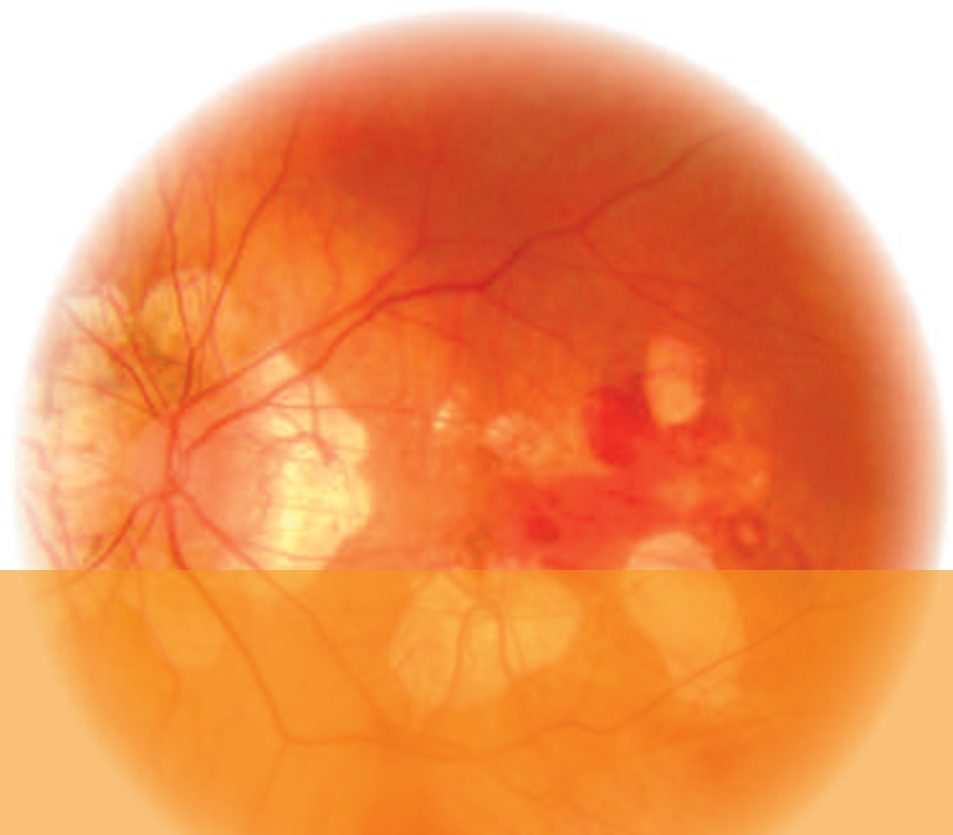
Therapeutic Dilemma 1

Only 30-50% of conventionally treated Graves' disease patients will remain in remission after withdrawal of antithyroid drugs, the other patients will relapse sooner or later and will need definite treatment (thyroidectomy or radiodine therapy). Therefore, an early classification is of major importance for physician and patient. Neither clinical symptoms nor euthyroidism are conclusive for this decision.

Laboratory diagnostic approach

Earlier investigations – even when the highly sensitive TRAK human assay was used – have shown that TRAb titers will not predict relapse for the individual patient.^{3,11} However, in these studies the same TRAK human cut off levels were used as for the **diagnostic assignment**, namely 1.5 IU/L. More recent studies revealed a reliable **prognostic value** of the TRAK human measurement by using higher cut offs.

NOTE: The following data were determined using the Thermo Scientific B·R·A·H·M·S TRAK human. The results should not be used with other assay systems.





Facts

Schott^{16,17,18} and Quadbeck^{14,15} demonstrated that TRAK human levels above 10 IU/L as early as 6-12 months of antithyroid drug therapy forecast a relapse with high significance (see Fig. 2).¹⁶ The positive predictive value was found to be 96.4%.¹⁶ The differentiation between stimulating and blocking TSHR autoantibodies by bioassays was of no additional value for the prognosis.¹⁷

In another group of patients an “end of treatment cut off” (18-42 months) TRAK human of 3.85 IU/L had a prognostic value for relapse with a sensitivity of 85.3% (specificity 96.5%).⁵

However, all three authors stated that TRAK human titers below these cut offs have no prognostic value for remission of Graves' disease.

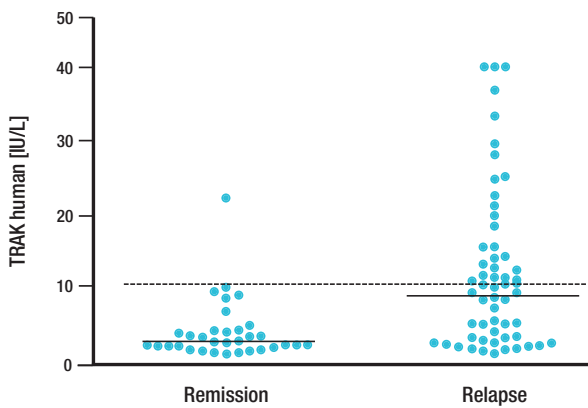


Figure 2 Distribution of TRAK human serum levels

Case report from practice

23 year old woman, Graves' disease, 4 weeks after withdrawal of antithyroid drugs after a 12 months course, normal thyroid volume, non-smoker, TSH 0.4 mIU/L, no eye signs, subjectively free from symptoms

TRAK human 12 IU/L ▶ strong probability for relapse ▶ thyroidectomy recommended

Graves' Ophthalmopathy (GO)

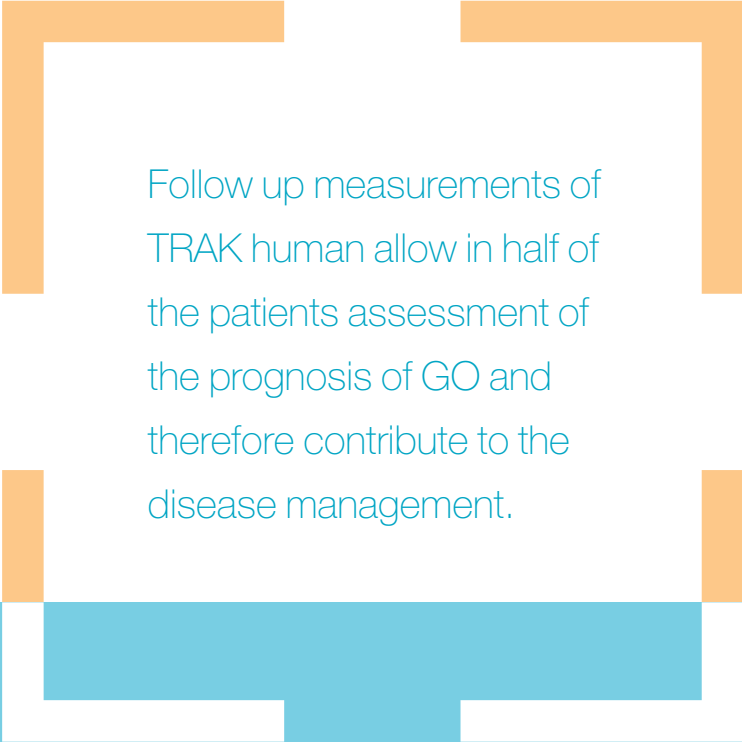
Mild or severe course to be expected?

Therapeutic Dilemma 2

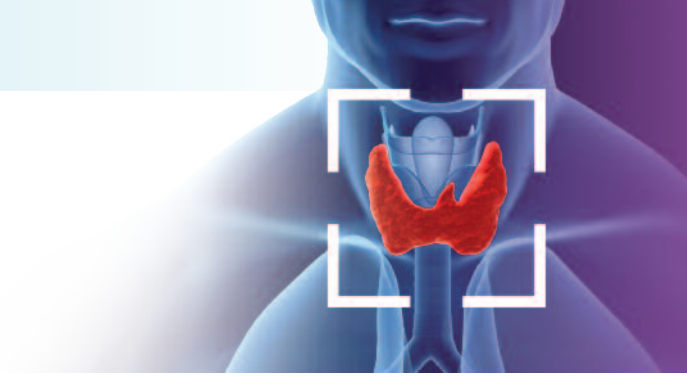
The reliable prognosis of severity and course of GO on the basis of the various known risk factors (goiter size, smoking, severity of hyperthyroidism, age) is still difficult. More than 50% of patients improve with thyreostatic therapy alone whilst patients with a severe course of GO need additional treatment of their eye disease with steroids and irradiation if necessary. Is it possible to predict the course of the GO for the individual patient?

Laboratory diagnostic approach

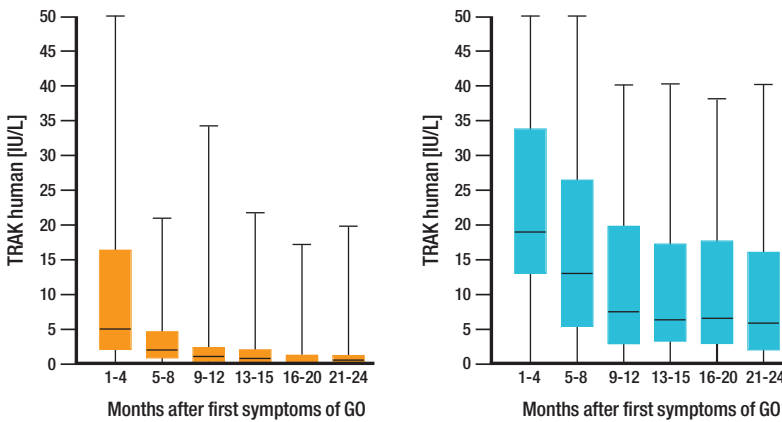
Eckstein et al. were investigating the correlation of TRAK human serum levels and the course of GO during the first 2 years after GO onset, and could show that TRAK human titers are associated with the severity of GO.^{19,20}



Follow up measurements of TRAK human allow in half of the patients assessment of the prognosis of GO and therefore contribute to the disease management.



Facts



The differences in TRAK human serum levels between patients with mild and severe course of GO were substantial enough (see Fig. 3) to define cut off levels (see Table 1) over the entire course of the disease by ROC plot analysis. Values below or higher certain cut offs were associated with either a mild or severe course of GO (specificity 90%).

Figure 3 TRAK human serum levels for

■ mild GO
■ severe GO

Time point: Months after GO onset	TRAK human cut off [IU/L] for prediction of a mild course	Odds ratios	TRAK human cut off [IU/L] for prediction of a severe course	Odds ratios
1-4	5.7	13.9	No prediction	–
5-8	2.6	6.8	8.8	18.4
9-12	1.5	3.7	5.1	16.9
13-16	1.5	15.6	4.8	14.3
17-20	1.5	2.3	2.8	31.1
21-24	1.5	14.7	2.8	8.7

Table 1 TRAK cut off values for the prediction of mild and severe GO

Case report from practice

63 year old woman, heavy smoker, Graves' disease, 6 months ATDT, now euthyroid, thyroid enlarged (43 mL), eye signs for 4 months, still edema, still impaired eye motility, significant improvement after steroids, no relapse

TRAK human 16 IU/L. Wait and see or continuation of therapy?

► Further treatment since patient is still at risk to develop severe course of GO!

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The gold standard Exceptionally fast and easy

The immunoassay **Thermo Scientific B·R·A·H·M·S TRAK human** is the gold standard for differential diagnosis and follow-up in Graves' disease and Graves' ophthalmopathy. Its high diagnostic sensitivity and specificity is now available on the immunoanalyzer **Thermo Scientific B·R·A·H·M·S KRYPTOR compact PLUS** allowing to determine TSH receptor autoantibodies (TRAb) exceptionally precise, fast, and easy.

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