

Accuracy of magnetic resonance imaging in diagnosing thyroid cartilage and thyroid gland invasion by squamous cell carcinoma in laryngectomy patients

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Abstract

Objectives: We examined the accuracy of magnetic resonance imaging in assessing thyroid cartilage and thyroid gland invasion in patients undergoing total laryngectomy for squamous cell carcinoma, by comparing histopathology results with imaging findings.

Study design: A retrospective study reviewed histology and magnetic resonance scan results for all total laryngectomies performed between 1998–2008 at University Hospital Aintree, Liverpool.

Methods: Pre-operative magnetic resonance images were reviewed independently by two consultant head and neck radiologists masked to the histology; their opinions were then compared with histology findings.

Results: Eighty-one magnetic resonance scans were reviewed. There were 22 laryngectomy patients with histologically verified thyroid cartilage invasion and one patient with thyroid gland invasion. There were 31 patients with apparent radiological thyroid cartilage invasion pre-operatively (with 17 false positives), giving sensitivity, specificity, and positive and negative predictive values of 64, 71, 45 and 84 per cent, respectively. On assessing thyroid gland invasion, there were nine false positive scans and no false negative scans, giving sensitivity, specificity, and positive and negative predictive values of 100, 89, 10 and 100 per cent, respectively.

Conclusion: Magnetic resonance scanning over-predicts thyroid cartilage and gland invasion in patients undergoing total laryngectomy. Magnetic resonance scans have limited effectiveness in predicting thyroid cartilage invasion by squamous cell carcinoma in laryngectomy patients.

Key words: Total Laryngectomy; MRI scans; Thyroid Cartilage; Thyroid Gland

Introduction

The diagnosis of thyroid cartilage and/or thyroid gland invasion in patients presenting with squamous cell carcinoma (SCC) of the larynx and/or hypopharynx is an important factor in the management decision-making process. Thyroid cartilage invasion is associated with a lower response rate to radiation therapy and a higher risk of tumour recurrence.¹ Consequently, accurate assessment of any thyroid cartilage invasion by the tumour is vital for staging and treatment.

For example, the presence of comprehensive thyroid cartilage invasion would be staged as tumour stage four (T₄), using the tumour–node–metastasis staging system,² indicating a significant survival disadvantage.³

In contrast to the relatively common finding of thyroid cartilage invasion by SCC, the incidence of thyroid gland invasion is reported to be low. A recent

literature review revealed an 8 per cent incidence of thyroid gland invasion in patients undergoing laryngectomy for laryngeal carcinoma.⁴ The prognostic significance of thyroid gland invasion is less well documented, although the available data suggest that patients presenting with laryngeal or hypopharyngeal SCC with thyroid gland invasion have worse survival outcomes.⁵ Therefore, the importance of correctly diagnosing thyroid gland invasion is paramount as it too has implications for treatment options and outcome.

It is important to note that there are benefits to patients of preserving at least one thyroid lobe following total laryngectomy. To do so obviates the need for life-long thyroxine supplementation, and minimises significantly the risk of hypocalcaemia and its attendant morbidities. Hence, if total thyroidectomy can be avoided, it should be.⁶

Two radiological modalities, computed tomography (CT) and magnetic resonance imaging (MRI), are routinely employed in the staging investigations of patients presenting with cancer of the larynx and/or hypopharynx. Both techniques are used in the assessment of thyroid cartilage and/or thyroid gland invasion.

Although CT scans are still widely used, they are not as sensitive as MRI, and tend to underestimate cartilage invasion.^{7,8} However, MRI tends to over-diagnose tumour invasion of the thyroid cartilage.^{7,9,10}

This over-diagnosis has been attributed to reactive inflammation due to the underlying pathological process. As a consequence, the specificity and positive predictive values of MRI remain low in this context. Previous papers have reported small case studies and have used various radiological criteria to diagnose thyroid cartilage or gland invasion. Therefore, in light of this contradictory evidence, our aim was to assess the sensitivity, specificity, and negative and positive predictive values of MRI in predicting thyroid cartilage and/or thyroid gland invasion in patients presenting to our large, centralised, tertiary referral head and neck cancer centre.

Method

A retrospective review was undertaken of all those patients who had undergone a total laryngectomy, with or without partial pharyngectomy, at the University Hospital Aintree between 1998 and December 2008. A list of patients was collected from the Liverpool head and neck database, pathology and multidisciplinary team meeting databases, operating theatre logbooks, and coding databases.

Patients were included if they had undergone a total laryngectomy for *de novo* SCC originating in the glottis, supraglottis, subglottis or hypopharynx. Patients were excluded from the study if they had undergone a laryngectomy for non-oncological indications. Patients who had been previously treated with external beam radiotherapy (i.e. presenting with recurrent tumours) were included, but this information was not revealed to the radiologists assessing the scans.

Following compilation of the patient list, post-resection histopathology reports and pre-operative staging scans were retrieved.

Although the histopathology reports were available for nearly all patients, pre-operative staging MRI scans were not. The main reason for this was logistical. Over recent years, a digital computerised X-ray, picture archiving and communication system had been installed in our establishment. Scans performed following the introduction of this system were easily retrieved, whereas hard copy scans pre-dating the introduction of this system were much harder to obtain. In addition, during the early part of the study period, many scans were performed in hospitals peripheral to our tertiary referral centre. The retrieval of these scans proved impossible.

Once obtained, the scans were independently reviewed by two consultant radiologists with a specialist interest in head and neck imaging. In addition to the radiologists being masked as to whether patients had previously been treated with external beam radiation, they were also masked to the histopathology reports generated following surgical resection. Their specific task on reviewing the scans was to comment on thyroid cartilage and thyroid gland invasion.

The criteria used to diagnose thyroid cartilage invasion comprised one or more of the following: (1) low signal on T1-weighted images, (2) high signal on short inversion recovery (STIR) sequence adjacent to the tumour and (3) tumour on both sides of the thyroid cartilage.

The criteria used to diagnose thyroid gland invasion comprised one or more of the following: (1) high signal on short inversion recovery (STIR) sequence adjacent to the tumour, (2) low signal on T1-weighted images and (3) tumour invading the thyroid gland.

Radiological findings were then compared with histological findings. Following this comparison, the sensitivity, specificity, and negative and positive predictive values for the effectiveness of the MRI in diagnosing thyroid cartilage and/or gland invasion were calculated.

Results

A total of 194 patients underwent a total laryngectomy at University Hospital Aintree, Liverpool, UK, between January 1997 and December 2008. Of these 194 patients, seven had received pre-operative radiotherapy; these patients were included in the study. One hundred and thirteen patients were excluded: three had a laryngectomy for non-oncological indications; eight were staged using CT scans rather than MRI; and 102 magnetic resonance scans were unavailable.

Therefore, 81 magnetic resonance scans were available for review. The mean patient age was 60 years, with a range of 17–88 years. There were 72 men and nine women.

Figure 1 depicts the primary tumour site for each laryngectomy case. The majority of tumours originated from the glottis (42 of 81, 52 per cent).

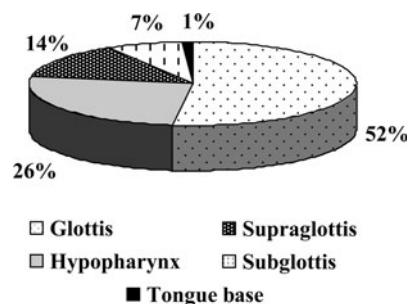


FIG. 1

Site of primary tumour for all patients.

TABLE I
THYROID CARTILAGE INVASION RESULTS: ALL PATIENTS

MRI result	Histology result		Total
	Positive	Negative	
Positive on MRI	14	17	31
Negative on MRI	8	42	50
Total	22	59	81

Data represent patient numbers. MRI = magnetic resonance imaging

Thyroid cartilage invasion

On reviewing the histopathology reports, 22 specimens had evidence of thyroid cartilage invasion. In contrast, the radiologists considered that there was radiological evidence of thyroid cartilage invasion in 31 cases (Table I).

Consequently, the sensitivity, specificity, and positive and negative predictive values of MRI in detecting tumour invasion of the thyroid cartilage in this series were 64, 71, 45 and 84 per cent, respectively.

Interestingly, all of the seven salvage total laryngectomy cases included were considered to show radiological evidence of thyroid cartilage invasion (Table II). Histopathological examination confirmed however that in only four specimens was there evidence of thyroid cartilage invasion. Consequently, in this small but clinically important subgroup, the sensitivity of MRI with respect to thyroid cartilage invasion was 100 per cent, while the specificity dropped to 50 per cent.

If patients undergoing salvage surgery are excluded (Table III), the specificity of MRI improved slightly (74 per cent), with a corresponding decrease in sensitivity (62 per cent). In contrast, the positive predictive value (48 per cent) and negative predictive value (83 per cent) were in keeping with the values calculated for the complete dataset.

Thyroid gland invasion

As part of their surgical procedure, 20 (25 per cent) patients had a total thyroidectomy whereas 48 (59 per cent) had a hemi-thyroidectomy. In the 13 cases in which the thyroid gland was preserved, there was no

TABLE II
THYROID CARTILAGE INVASION RESULTS: POST-RADIOTHERAPY PATIENTS ONLY

MRI result	Histology result (n)		Total
	Positive	Negative	
Positive on MRI	1	3	4
Negative on MRI	0	3	3
Total	3	6	7

Data represent patient numbers. MRI = magnetic resonance imaging

TABLE III
THYROID CARTILAGE INVASION RESULTS WITH SALVAGE SURGERY PATIENTS EXCLUDED

MRI result	Histology results (n)		Total
	Positive	Negative	
Positive on MRI	13	14	27
Negative on MRI	8	39	47
Total	21	53	74

Data represent patient numbers. MRI = magnetic resonance imaging

pre-operative radiological indication of thyroid gland invasion by tumour.

In 10 cases, pre-operative radiological evidence of thyroid gland invasion was present. However, in only one case was invasion confirmed histopathologically (Table IV). Consequently, the sensitivity, specificity, and positive and negative predictive values of MRI in detecting tumour invasion of the thyroid gland in this series were 100, 89, 10 and 100 per cent, respectively.

Discussion

An accurate assessment of thyroid cartilage and gland invasion is important for pre-therapeutic staging of laryngeal carcinoma. Should such invasion be present, it will have significant prognostic implications and may well influence the treatment offered.

It has been previously documented that both CT and MRI have limitations in predicting tumour involvement in the thyroid gland and/or cartilage.¹¹ Computed tomography can miss minor or early cartilage invasion, due to the normal irregular patterns of calcification and ossification of thyroid cartilage,¹² and MRI can demonstrate details of non-ossified and ossified cartilage better than CT.¹³

When CT and MRI have been directly compared in the detection of thyroid cartilage invasion, MRI has been shown to be more accurate and significantly more sensitive,⁷ although it over-predicts thyroid cartilage invasion. This has been attributed to reactive inflammation, oedema and fibrosis secondary to the underlying pathological process, which cause similar radiological appearances to those seen when thyroid cartilage is infiltrated by tumour.^{1,14}

TABLE IV
THYROID GLAND INVASION RESULTS: ALL PATIENTS

MRI results	Histology results		Total
	Positive	Negative	
Positive on MRI	1	9	10
Negative on MRI	0	71	71
Total	1	80	81

Data represent patient numbers. MRI = magnetic resonance imaging

In our study, MRI had a higher specificity than sensitivity when used to assess thyroid cartilage invasion. While MRI over-predicts cartilaginous involvement, the corollary is that it has a more reliable negative predictive value. For example, if MRI predicts non-involvement there is an 84 per cent chance that this is true.

It is interesting to note that the sensitivity and specificity values calculated from our data are in general lower than those previously reported.^{8,14} This may be a consequence of our large tertiary referral practice, in which our radiologists almost exclusively report on head and neck images and our pathologists almost exclusively report on head and neck tissue samples.

- **We examined the accuracy of magnetic resonance imaging (MRI) in assessing thyroid cartilage and thyroid gland invasion in patients undergoing total laryngectomy for squamous cell carcinoma**
- **Specificity was higher than sensitivity for detecting thyroid cartilage invasion**
- **Cartilaginous involvement was over-predicted, but negative predictive value was more reliable**
- **Thyroid cartilage invasion was over-predicted, attributed to reactive inflammation, oedema and fibrosis secondary to the underlying pathology**
- **In patients with laryngeal carcinoma, pre-operative MRI did not reliably detect thyroid gland invasion**

Of the 20 total thyroidectomies and 48 hemi-thyroidectomies performed in our series of 81 laryngectomies, only one case had histologically confirmed thyroid gland invasion. This constitutes an incidence of 1.2 per cent, lower than that reported in a recent systematic review of eight case series, which showed an overall incidence of thyroid gland invasion of 8 per cent in laryngectomy patients.⁴

Although we demonstrated a sensitivity of 100 per cent and specificity of 89 per cent, the positive predictive value was only 10 per cent. Thus, there was an over-prediction of thyroid gland invasion. This high false positive rate is assumed to be due to peri-tumoural inflammation and oedema.¹⁴

It has been previously demonstrated that patients with subglottic extension have a higher incidence of thyroid gland invasion.¹⁵ This is thought to be because tumours situated at the anterior angle of the thyroid cartilage and the cricothyroid membrane have a greater propensity to spread outside the larynx.¹⁶ However, the one patient in our group who was shown to have invasion of the thyroid gland presented with a glottic primary tumour. Furthermore, of the six patients who underwent laryngectomy for subglottic carcinoma, none had direct invasion of the thyroid

gland. In none of these cases did the MRI suggest direct invasion pre-operatively.

Conclusion

Our data suggest that MRI is not a reliable method of detecting thyroid gland invasion pre-operatively in patients presenting with laryngeal carcinoma. Therefore, MRI findings should not, in most instances, be used to decide whether to remove part or all of the thyroid gland as part of total laryngectomy. In light of these data, and in the knowledge that thyroid gland invasion in the context of laryngeal carcinoma is relatively rare,⁴ it is our opinion that the decision to perform a total thyroidectomy or hemi-thyroidectomy during laryngectomy should rely on the presence of suspicious intra-operative findings, such as the close proximity of carcinoma, and should not be based on pre-operative MRI findings.

Similarly, surgeons should remain aware of the fact that pre-operative MRI will often over-predict thyroid cartilage invasion. Although this is of little importance when faced with a clinical scenario that mandates total laryngectomy, it is of enormous significance if partial, function-sparing laryngeal surgery is being considered, particularly transoral laser microsurgery. Reliance on the findings of pre-operative MRI in these circumstances may easily result in over-treatment. Consequently, it is also our opinion that treatment judgements in these particular cases should rely on clinical assessment rather than MRI results.

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