uPA was 1.11±2.71 ng/mg protein, median uPA 0; range [0.0–10.0], mean PAI-1 15.04±29.45 ng/mg protein, median PAI-1 4.31; range [1.35–136.70]) compared to normal thyroid tissue (mean uPA 0.004±0.147 ng/mg protein, median 0; range [0.000–0.060], mean PAI-1 2.34±0.35 ng/mg protein, median 2.33; range [1.52–3.00]). There was a positive correlation between the levels of uPA and PAI-1 concentrations in cancerous tissue ($p < 0.001$, correlation coefficient 0.72). Both uPA and PAI-1 levels were associated with carcinoma differentiation, larger tumor size and these two proteins exhibited distinct rise if distant metastasis were present. The uPA and PAI-1 levels showed significant difference among various histological type of thyroid cancer. However no significant association between uPA and PAI-1 levels and extrathyroid invasion was found.
These data suggest that significant correlations exist between uPA and its inhibitor PAI-1 and the standard prognostic parameters in thyroid cancer. Further investigations have to clarify whether uPA and PAI-1 could be independent prognostic factors in thyroid cancer.

1075 POSTER

P53 and Ki-67 expression in distinguishing follicular adenoma from follicular carcinoma of thyroid

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Background: Distinguishing between follicular adenoma and follicular carcinoma of the thyroid can be particularly challenging when performing routine diagnostic pathology, and often requires the examination of several histological sections in order to identify the presence of unequivocal capsular and/or vascular invasion.
Material and methods: To investigate the use of immunohistochemical markers in the differential diagnosis of follicular lesions of the thyroid, we studied the expression of P53 and Ki-67 in 52 follicular adenomas and 52 follicular carcinomas of the thyroid. As a control, we examined 30 simple goiters.
Results: Ten percent (10%) of simple goiters exhibited nuclear P53 expression, compared with 55.8% for follicular adenomas, and 82.7% for follicular carcinomas. Nuclear Ki-67 expression was observed in 30% of simple goiters, 51.9% of follicular adenomas and 96.2% of follicular carcinomas. The sensitivity and specificity of using p53 to diagnose follicular carcinoma from follicular adenoma was 82.7% and 44.2% respectively, while for Ki-67 the sensitivity and specificity was 96.2% and 48.1% respectively. When analyzing both markers together the sensitivity and specificity was 82.7% and 57.7% respectively.
Conclusions: The results of this study indicate that immunohistochemical detection of P53 and Ki-67 may have practical utility in the differential diagnosis of follicular carcinomas from follicular adenomas in routine thyroid surgery.

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Validation of dynamic contrast enhanced MRI parameters as surrogate markers of hypoxia in squamous cell carcinoma of the head and neck

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Background: Hypoxia is an important determinant of response to radiotherapy and correlates with outcome in squamous cell carcinoma of the head and neck (HNSCC).
A non-invasive method for identifying areas of reduced oxygenation within tumours may enable radiotherapy planning and delivery to be individually optimised.
Aim: To validate established parameters derived from dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) as surrogate markers of hypoxia in squamous cell carcinoma of the head and neck (HNSCC).
Methods: 144 measurements of DCE-MRI parameters from 12 regions of interest (ROIs) were made in 4 patients with HNSCC prior to surgical resection. Examinations were performed on a 1.5 T Philips Intera®. An axial 3D scan at the centre of the tumour (TR = 4 ms, TE = 1.23, flip angle=2º) comprising 15.2 mm contiguous slices was followed by a geometrically identical DCE scan (TR = 4 ms, TE = 1.23, flip angle=10º) repeated continuously over 72 6.4 sec time-points. On the 10th repetition 0.1 mmolkg^{-1} of Magnevist®, was administered intravenously (iv) at a rate of 4 ml/sec. Scans were calibrated so intensity changes due to the passage of contrast agent were converted to changes in contrast concentration. Data were processed to produce quantitative contrast concentration curve descriptors (area under the curve, AUC; time to peak, TTP; time to onset, T1onset) and kinetic parameters associated with permeability (Ktrans, Kep) and extra-cellular, extra-vascular space (Ve). 0.5 g/m^2 pimonidazole hydrochloride was administered iv 16–20 hours before surgery. At resection the tumour was orientated such that the pathological specimen was sectioned in the image plane. The pimonidazole uptake was identified by immunohistochemistry. A histological section within the tumour was matched to the corresponding image slice and corresponding ROIs drawn on both the image slice and the section. The percentage of pimonidazole staining within the ROIs defined the hypoxic fraction. Correlations between the DCE-MRI parameters and the hypoxic fraction were assessed using the Spearman rank correlation coefficient (Rs).
Results: See Table 1.

DCE-MRI parameter	Ktrans	Kep	Ve	T1onset	AUC	TTP
Rs	0.753	0.595	−0.38	−0.231	0.697	−0.306
(Rs 95%CI)	0.298 to 0.929	0.013 to 0.876	−0.79 to 0.266	−0.72 to 0.411	0.187 to .911	−0.757 to 0.342
P-value (2-tailed)	0.00	0.05	0.24	0.44	0.01	0.36

Conclusion: These preliminary results suggest that pharmacokinetic parameters derived from DCE-MRI may be surrogate markers of hypoxia in HNSCC. This non-invasive, spatial mapping of intratumoural hypoxia may enable targeted radiation dose escalation to radioresistant clonogens with the potential for improved local control and survival in this group of patients.

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The significance of stromal desmoplasia and the appearance of myofibroblasts at the invasive front in squamous cell carcinoma of the oral cavity

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Background: The phenomenon of tumor invasion into the extracellular matrix in stroma has gradually been clarified to involve ingenious interactions between tumor and stromal cells. However, the underlying mechanisms of tumor desmoplasia and its biological significance in tumor growth, i.e., as a host defense mechanism or a scaffold for tumor invasion, remain unclear. Myofibroblasts has known to be a major player for fibrosis or constitution in granulation tissue. We examined extent to which the connective tissue in tumor stroma vary due to the histological grade of malignancy, and whether myofibroblasts play a role in assisting cancer invasion and metastasis.
Material and methods: Biopsy materials from 84 patients who had not yet undergone any treatment for oral squamous cell carcinoma (OSCC) and 11 samples of normal oral mucosa were used in this study. The data of semi-quantification analysis for intra-stromal collagen fiber which was performed by color distinguish technique using digital image of Azan staining and that of the immunohistochemical identification of myofibroblasts characterized with smooth muscle actin, vimentin, and desmin at the invasive front, was compared to clinicopathological parameters (mode of cancer invasion: Grade 1–3/4C/4D, degree of differentiation: low/moderate/high, T-categories: T1–4, pathological lymph nodes metastasis: pN+/−).
Results: Image analysis of stromal collagen fiber with regard to the histological mode of cancer invasion showed a unique feature with two peaks of both ends (normal control and grade 4D). In particular, there were few myofibroblasts in the low invasive mode (Grade 1–2), while myofibroblast-positive cases showed a significant increase from a moderate to high invasive mode (Grade 3–4D) ($p < 0.01$). Myofibroblast-positive cases were significantly increased along with the degree of differentiation ($p < 0.05$). Lymph node metastasis was found at a higher incidence among myofibroblast-positive cases than among negative cases ($p < 0.05$).
Conclusions: Fibrous stroma in OSCC showed a desmoplastic response, indicating an invasion protection system and tissue reconstruction as shown in grades 1 to 4C, whereas it is suggested to acquire an independent invasive mechanism in grade 4D that is essentially different from that in other grades, indicating the most frequent failure of loco-regional control, and tumor desmoplasia is one part of the stromal representation forms in highly-developed invasive tumors.