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Contributions to the improvement of the quality of the images in our system of computer-aided thermography of contact

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Purpose: The paper presents results obtained by the authors during the last 10 years in the field of contact thermography (CATE). They demonstrated that their own apparatus and their own computer-aided protocol is more efficient, comparing to the previous, in examinations both of superficial and deep cancers.

Methods: Stronger efficiency of CATE was obtained using: (1) picking up of more data in a stationary position and (2) by displacing the thermal sensors along the skin. Using PC and very precise methodology, the thermal map of the investigated area was obtained. Very important is the fact that our method allowed deep tissue thermal analysis, so any internal or superficial tissues could be investigated.

Results: The original apparatus and method CATE enables a non-invasive exploration of the functionality of the whole body, allows many re-examinations, with the lowest costs. In fact, aspects of energetic and metabolic processes could be stored and compared at different time intervals, both for normal and pathological conditions. The CATE system seems to be a real challenge in exploring molecular level of cellular phenomena. The presented apparatus and method could be used for: detection, screening, diagnose, treatment and post-therapeutical follow-up. Further improvements were done: the mathematical processing of thermogenesis values, for obtaining (a) tomo-thermography and (b) phono-thermography.

Conclusions: We appreciate that the above presented apparatus and method could represent a very useful investigating tool, particularly in the oncological field, but also in some clinical and experimental investigations.

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Detection of p53 gene alterations in saliva and brush cytological specimens from oral carcinoma risk patients

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Purpose: In oral cavity the epithelial cells are frequently removing and exfoliated cells might be detected in saliva and brush specimens. Recurrence and multifocal nature are the most important characteristics of oral cancer and so the identification of genetic alterations, like p53 mutations, in saliva of high-risk patients suggests possibilities for future oral cancer non-invasive screening technique.

Methods: We analyzed two groups of patients at risk of developing a new or recurrent oral carcinoma; one group had a leukoplakia for the first time (20 individues) and the other had a leukoplakia and previously one or two oral carcinomas (20 individues). The samples collected from each patient were: saliva, hair with root and a brush swabbed over the leukoplakia lesions. DNA was extracted from the cells of these samples and exons 4-8 of p53 gene were amplified. The PCR products were analyzed for mutations by SSCP and the bands having the highest probability to contain mutated alleles were carefully cut and the DNA fragments recovered from polyacrilamide gels to be sequenced with the aim of confirming and localizing the mutation.

Results: We identified p53 mutations in saliva and brush citologies from patients at risk of developing an oral carcinoma. 11 of 40 patients evaluated have one or two mutations in p53 gene; 7 of 20 patients with previous carcinoma showed mutations which were present both in saliva and brush. P53 mutations were observed too in 4 of 20 patients without previous carcinoma but only were present in brush cytologies. The mutations detected in saliva and brush correspond to the first group of patients and two of these patients have two mutations in exons 5 and 8 of p53 gene. In the patients with risk of the primary oral carcinoma the mutations were detected only in the brush sample. The mutations are found majority in exons 5 and 8, only one in exon 7 and a polymorphism in exon 6.

Conclusions: These results suggest that inactivation of p53 can be detected using oral cytologies specimens of patients with leukoplakias before malignant lesions are clinically apparent. The presence of p53 mutation in saliva would suggest recurrence. This technique is non -invasiveness, painless, rapidity and may be useful for the follow-up of these patients because of the risk of developed an oral cancer or a recurrence. In conclusion, this technique introduces new possibilities of analysis of tumor-specific molecular markers.

This work was supported by grants from the University of the Basque Country (UPV I02-EA134/96), UPV I02.I02-TB 128/97; the Basque Government (PI-97/27) and FIS project/Basque Government Department of Health (99/09409)

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Initial report of the HER2000 study: a multinational study of her2 status of breast cancer using immunohistochemistry (IHC; Herceptest)

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Background: HER2 is an important prognostic and predictive marker in breast cancer, with a HER2-positive status being indicative of aggressive disease, decreased survival and eligibility for the HER2-specific monoclonal antibody Herceptin. Furthermore, it is widely accepted that routine testing for HER2 status is essential for optimal breast cancer management. Until now, no study has examined HER2 status on a global scale. Therefore, we used IHC to obtain epidemiological data on HER2 status in 10 countries worldwide.

Methods: Formaldehyde-fixed, paraffin-embedded sections (3-5 μm) of samples from primary breast tumours or metastases were retrospectively or prospectively tested for HER2 status using the standardised HercepTest IHC kit. All samples were scored 0, 1+, 2+ or 3+ according to standard criteria outlined in the package insert for HercepTest. Some samples were also stained by IHC using other antibodies; these tests were assessed by individual laboratories as negative or positive.

Results: Data are currently available for the initial 4,476 of 10,500 samples tested; 98% were from primary tumours and 90% were fixed in neutral-buffered formalin. Mean patient age was 59.2 years. By the HercepTest, HER2 status was scored as 0 in 46% of samples; 1+ in 26%; 2+ in 14%; and 3+ in 14%. Subsets of these sections were tested by non-standardized IHC staining procedures using a polyclonal anti-HER2 antibody (A0485) on 814 specimens and the mouse anti-HER2 monoclonal antibody CB11 on 1077 specimens. These tests produced higher positivity rates than the HercepTest: 39-45% and 21-53%, respectively. Interestingly, 91% (269/296) of HercepTest 3+ samples for which alternative IHC test results were available were positive on these tests; 83.5% (1324/1584) of HercepTest 0 or 1+ samples were negative on alternative tests. Variation in scores between countries and centres was noted for all tests, except for the HercepTest in Germany.

Conclusions: The overall rates of HER2 positivity obtained using the HercepTest in this study are consistent with those observed in smaller studies. The reproducibility of HercepTest results between centres in Germany may reflect the existence of an established quality assurance programme. These results indicate the importance of HER2 test validation, strict adherence to test protocols and quality control programmes to ensure that HER2 status is determined correctly and the appropriate patients are selected for Herceptin therapy.

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Molecular imaging paradigms and cancer therapy

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Imaging paradigms can be used to enhance the scientific impact of cancer trials. This lecture will focus on the development of imaging paradigms to measure hypoxia, proliferation, angiogenesis, gene expression and enzyme function.

Hypoxia occurs to a variable extent in tumours and is an important determinant of therapeutic response and survival. We have developed SR 4554 as a magnetic resonance spectroscopy (MRS) and positron emission tomography (PET) compatible probe for the measurement of hypoxia. The design features of SR 4554 were consistent with its *in vivo* pharmacokinetics, enzymology of bioreduction, subcellular distribution in spheroids and tumour retention. Differential retention was demonstrated in tumours with different radiobiological hypoxic fraction and following modulation by carbogen and hydralazine. Based on its interesting properties, SR 4554 has been selected for clinical development and is now in Phase 1 trials.

There is the need to develop new assays, which can be used to evaluate novel mechanism-based cytostatic agents in patients. We are developing 2-[^{11}C]thymidine and 2'-[^{18}F]fluorothymidine for measuring antiproliferative