The resonance that can be observed arise from natural stable isotopes in these compounds, mostly those of ^{1}H, ^{31}P, ^{19}F and ^{13}C. Because of some limitations inherent to the MR technique such as sensitivity, the use of MRS in vivo usually is restricted to a set of small metabolites, which are present at tissue levels of more than about 0.1 mM. These are metabolites that play important roles in energy metabolism (e.g., ATP, lactate) and in lipid metabolism (e.g., choline compounds, triglycerides). Furthermore, as resonance frequencies are also sensitive to physiological environment of the metabolites other parameters such as tissue pH can be determined by MRS. The nucleus of ^{19}F mostly has been used to monitor metabolism of drugs like 5FU and the nucleus of ^{13}C to follow metabolic fluxes as ^{13}C can be applied as a non-ionising label due to its low natural abundance.
The non-invasive nature of MR allows one to perform longitudinal metabolic and physiological examinations.
These properties of in vivo MRS have been exploited in numerous experimental studies in oncology.
Often in these studies the MRS investigations are combined with other information that can be obtained (simultaneously) by different MR approaches such as on blood flow or oxygenation. MR spectroscopy has also been applied to tissue biopsies or extracts of whole tumours or tumour cells, by which higher sensitivity and better spectral resolution can be achieved. The research that records and exploits metabolic profiles of tissues or cells by MRS or otherwise sometimes is referred to as metabolomics.
The use of MRS in cancer diagnosis is largely restricted to the use of the ^{1}H nucleus. This is the most sensitive nucleus (allowing the measurement of relatively small volumes and therefore the registration of tumour heterogeneity) and can be easily combined with (routine) clinical MRI approaches, which are based on the observation of the ^{1}H nucleus in body water. Although MRI is often able to record lesions that may represent tumour tissue it is generally difficult to make a differential diagnosis with respect to pathologies that cause similar types of lesions. As MRS may provide metabolic information that is more specific its use in tumour diagnosis was attempted already some time ago. Only in the last 5 years the technology of human MRS has evolved to such a level that this became possible in a clinical environment. The most important cancers in which MRS is now being used for diagnosis, grading and treatment evaluation are brain, prostate and breast tumours.
New developments in which MRS methods are involved that could be applied to tumour research and diagnosis, include the emerging field of molecular imaging combining different imaging modalities (although MRS can be considered as molecular imaging avant la lettre) and the use of hyperpolarisation to boost the sensitivity of MRS.

Scientific Symposium
Colorectal cancer can be prevented

66 INVITED

Colorectal cancer can be prevented: epidemiology and primary prevention

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Colorectal cancer is the second most common incident form of cancer in Europe and also the second most common cause of cancer death. Comparison of incidence and mortality rates over long periods of time clearly demonstrates that the mortality rates are declining at the same time as the incidence is rising. In the European Union, colorectal cancer mortality is fifty percent higher in men than in women and the mortality rate is higher in men than in women in each Member State of the European Union. The highest national mortality rates recorded in men are in Ireland, Denmark, Austria, Luxembourg and Germany. The lowest rates are recorded in Greece, Finland, Iceland and Sweden. The pattern is quite similar in women.
Colorectal cancer is clearly an important and increasing Public Health concern although there is room for optimism with respect to the possibility that prospects for the prevention of colorectal cancer could be found. It is clear that there are dietary components which can modify an individual's risk of colorectal cancer as can related lifestyle issues such as physical activity and overweight. While it is possible to be optimistic, there is still more research needed to identify the precise dietary components associated with colorectal cancer risk. When this is clarified, prospects for prevention will greatly improve although a balanced diet, rich in fruits and vegetables and fibre, with a general tendency for more fish and chicken rather than red and processed meat, accompanied by a sensible physical activity programme and achieving stability of body weight (for height), will almost certainly reduce the risk of colorectal cancer as well as of other chronic conditions.
The declines in the mortality rates from colorectal cancer in many (developed) countries in the presence of increasing incidence, represents a great advance in cancer control. This probably represents a success for increased awareness and (probably) subsequent stage drift over time; although there have been treatment advances these have mainly led to the most appropriate treatment being given to the most appropriate patient. However, successful primary prevention looks an attractive possibility in the not-so-distant future.

67 INVITED

Secondary prevention and screening for colorectal cancer (CRC) in the average risk population

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There are several options for CRC screening. Fecal occult blood testing (FOBT), by Haemoccult, is the most extensively examined method. This home-test kit requires collection of two samples from three consecutive stools, which are smeared onto cards and mailed to a laboratory for processing. Colonoscopy is recommended if any of the cards are positive since up to 50% will have a cancer or large adenoma. Biennial FOBT has been shown, in three randomised trials to reduce CRC mortality by a 15–20%. Immunochemical tests for haemoglobin or other blood components show greater sensitivity for both CRC and adenomas but at the expense of lower specificity. Flexible sigmoidoscopy (FS) is sensitive for the detection of distal adenomas. Three randomised trials are in progress. The protection afforded by a single FS may last for up to 10 years or even longer depending on the age at which it is undertaken. Two trials are examining the efficacy of a single FS at age 55–64. Colonoscopy screening at 10-yearly intervals from age 50 years is now considered the gold-standard test in the US. However data on the efficacy of colonoscopy in reducing proximal colon cancer rates and on the feasibility of offering 10-yearly high-quality, safe colonoscopy are lacking Potential future methods include examination of molecular markers in stool, and MRI and CT colonography, which are safer and better tolerated than colonoscopy. The sensitivity of both techniques for CRC and large adenomas seems high, although results vary by centre with a steep learning curve. If accuracy improves, costs reduced and the need for bowel-preparation eliminated, there may be a role in average-risk screening.

68 INVITED

Hereditary and familial colon cancer syndromes

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Although most colorectal cancers occur sporadically, about 25% arise in a familial context and 5 to 7% percent have an autosomal dominant inheritance and occur in genetically distinct high risk families. Colorectal cancers, whether sporadic or hereditary, are caused by a defined set of molecular events.
There are at least two different pathogenetic pathways for colorectal cancer: the chromosomal instability pathway and the microsatellite instability pathway; the two major inherited syndromes, familial adenomatous polyposis (FAP) and Hereditary non-polyposis colorectal cancer (HNPCC) are caused by germline defects in these pathways. These different pathways, however, converge on common pathological entities that have crucial functions in the regulation of normal crypt homeostasis. Further insight into colorectal tumorigenesis pathways can lead tot the development of useful prognostic indicators and target preventive and therapeutic strategies in the management of colorectal cancer.
Advances in the management of hereditary colorectal cancer syndromes have been principally due to advances in the understanding of the genetics of these syndromes. This has led to the possibility of preclinical genetic diagnosis and early surveillance and prevention strategies. In addition, improvement in medical and surgical management have also occurred. However, risk stratification is essential to the appropriate use of colorectal and extraintestinal cancer screening methods. Effective educational strategies that promote physician awareness regarding familial risk, risk assessment skills, and appropriate use of relevant screening guidelines are needed. Nevertheless, various vexing problems can deter the diagnosis and management of these syndromes, such as lack of medical and pathological documentation, poor cooperation of family members and/or their physicians, cultural barriers, economic issues, patient fear and anxiety.
This presentation will provide a overview of the hereditary and familial GI cancer syndromes, aiming to help clinicians in the recognition and management of this disorder. This can be a challenge, for instance the rapid advances in molecular medicine can be difficult to integrate in clinical practice. Hence we will also emphasize issues such as when and how to