Proton MRS of Skin Biopsies Distinguishes Melanoma from Benign Lesions

E. Hsiao[1], R. Bourne[1], J. Stretch[2], R. Scolyer[2], J. Thompson[2], C. Mountford[1], C. Lean[1]

[1]Department of Magnetic Resonance in Medicine, University of Sydney, Institute for Magnetic Resonance Research, Sydney, NSW, Australia, [2]Sydney Melanoma Unit, Royal Prince Alfred Hospital, Sydney, NSW, Australia

Introduction

Proton MRS of biopsy tissue analysed using an objective pattern recognition method, Statisitical Classification Strategy (SCS), accurately detects malignant pathology in a range of organs with sensitivity and specificity rates as high as 99% (1,2). More recently, MRS of FNA samples from excised lymph nodes from melanoma patients has been shown to accurately detect micrometastasis in these nodes (3). Here we apply proton MRS to distinguish primary melanoma from benign lesions based on changes in MR visible metabolite compositions. We postulate that MRS of biopsy will assist in the rapid and accurate diagnosis of melanoma, in particular in those instances where histological diagnosis is difficult.

Methods

Punch biopsy was performed on 27 skin lesions from 25 patients. Ten invasive melanoma and 17 benign skin biopsies were examined including 7 compound naevi, 2 intradermal naevi, 3 normal skin biopsies and 3 seborrheic keratoses. A punch biopsy was taken from the centre of each lesion prior to surgical excision. Skin lesions were excised after punch biopsy and submitted for detailed histopathological examination. All punch biopsy specimens were placed in 300 μL PBS/D_2O, snap frozen in liquid nitrogen and stored at –70^{o}C prior to proton MRS. Proton MRS (8.5T) was performed at 37^{0}C on a Bruker Avance AM-360 wide-bore spectrometer with a standard 5 mm dedicated proton probe-head in accordance with standard protocols (4). Bruker XWINNMR software was used to process the spectra. Integration of 14 regions subjectively selected on the basis of common peaks present in the spectra (Fig. 1) was performed after manual phase adjustment and baseline correction. Two class discriminant analysis was performed using "STATISTICA" software. Each biopsy was classified as either malignant or benign based on LDA of a training set comprising all biopsies except the lesion to be classified (Leave One Out method).

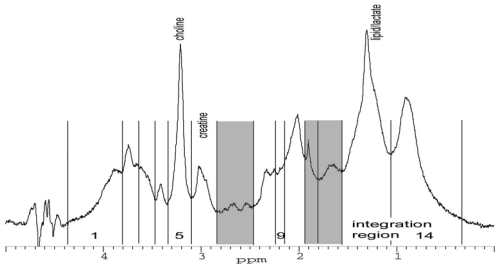
Results

The proton MR spectrum of a melanoma biopsy is shown in Figure 1. The 7th, 11th and 12th regions of the spectra (Fig. 1) were found by LDA to be optimal in discriminating melanoma from benign skin lesions. Using these three regions, all compound naevi, dysplastic naevi, seborrheic keratoses and normal skin biopsies were accurately identified as benign tissues. One intradermal naevus was falsely identified as a malignant lesion while another intradermal naevus was accurately classified as a benign lesion. In the melanoma group, only one out of 10 melanoma biopsies was incorrectly classified as a benign lesion.

Discussion

The three spectral regions optimal in discriminating malignant from benign skin lesions are consistent with signals from the amino acids aspartate, asparagine, methionine, lysine, leucine and isoleucine (4). 2D spectroscopy of biopsy tissue (not shown) support elevated levels of lysine, leucine and isoleucine being the main amino acids contributing to the discriminatory MR signals in melanoma tissue relative to benign tissue. It is noteworthy that an elevated choline signal (3.12-3.37ppm), which is conventionally considered indicative of malignancy, was not identified by LDA as discriminatory for melanoma.

Histopathology is the gold standard for the diagnosis of melanoma. However, a small portion of benign skin lesions can mimic melanoma both clinically and histopathologically. Altered biochemistry in melanoma allows MR spectroscopy to distinguish melanoma from benign lesions. This pilot study has demonstrated the potential of ex vivo MRS of skin biopsies to aid in the clinical management of melanoma patients by providing rapid and accurate diagnosis of melanoma. These findings will be further validated by correlating larger samples of various lesions including histopathologically overt melanoma, overt benign lesions, and melanocytic lesions of uncertain malignant potential with their clinical outcomes.



Conclusions

- Proton MRS of skin biopsy can identify melanoma with high sensitivity and specificity.
- Elevated lysine, leucine and isoleucine may distinguish melanoma tissue from benign.
- Elevated choline was not an identifying feature of the spectra from melanoma tissue.

Fig 1. The MR spectra were divided into 14 contiguous regions. LDA identified the integrals of the 7th, 11th and 12th regions (shaded) effective for discrimination between melanoma and benign skin tissue.

References

1. Lean et al., Ann Rep NMR Spec. 2002;48:71.
2. Mackinnon *et al.* Radiology 1997;204(3):661.
3. Lean et al, Melanoma Research 2003; 13:1-3.
4. Mackinnon et al.,World J. Surg. 1996; 20:841