Localized NMR Spectroscopy with a 1.5 T Whole-Body Imager Using CODEX

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With a whole-body NMR imager working at 1.5 T localized ^{1}H and ^{31}P spectra were obtained using the CODEX sequence. Examples are presented: With ethanol ^{1}H spectra the resolution, stability, and sensitivity are documented. Human *in vivo* investigations of the yellow bone marrow of $(13\ mm)^3$ volume elements show well resolved spectra with a good signal-to-noise ratio. An example for ^{31}P spectroscopy is also given.

Introduction and Method

Localized *in vivo* NMR spectroscopy is frequently applied in various fields of scientific research. Many different methods which allow the acquisition of fully localized spectra are used for this purpose [1–18]. Among these methods, CODEX [13] ("volume selection by CODed slice EXcitation") is a subtraction method which is well suitable for ^{1}H and ^{31}P as well. CODEX combines the advantages of ISIS [5] and DRESS [19] as a short T_2-sensitive time, a relatively small volume of which the acquired signal stems from and a full localization.

Volume selection with CODEX is achieved by four single experiments. The principle of the method and the corresponding subtractions are shown in Figure 1. All four experiments produce different signals of the same slice, here e.g. a z-slice. The difference between them is the different coding of the magnetization within these slices. This coding process is based on the same principles as used by the ISIS [5] method. A final subtraction $(S1-S2)-(S3-S4)$ of the signals results in a signal which has its origin only in a well defined volume of interest (VOI). All other signals are cancelled. Figure 2 shows the pulse and gradient sequences of the four experiments and the corresponding subtraction scheme. In all four experiments a 90° pulse in presence of a z-gradient results in a slice selective signal. The gradient refocusing is done immediately afterwards. The time from the center of the pulse to the beginning of the data acquisition is minimal 3 ms. For this, constant and frequency dependent phaseshifts can occur which are well known from the DRESS [19] method. Before the 90° pulse the coding process takes place by the application of none, one, or two 180° slice selective inversion pulses. The slice selection gradients of these inversion pulses are prolonged for 3 ms to destroy unwanted signals. In addition an expanded phase cycling scheme is applied in experiments with 4×2 acquisitions or more [13].

The CODEX method has two advantages over the ISIS method. Firstly, the relation between the volume

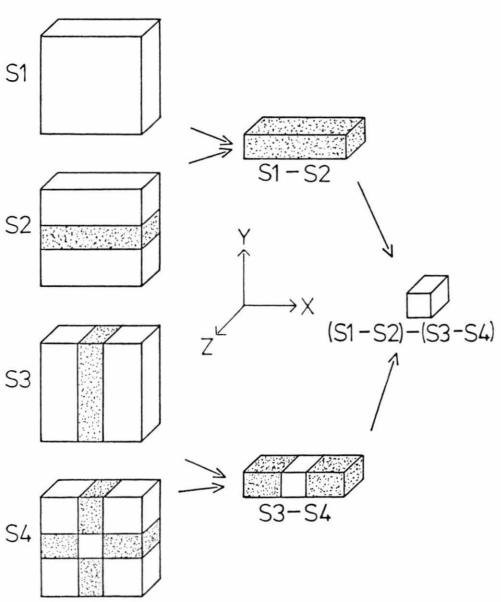

Fig. 1. Schematic representation of the principle of CODEX. Four experiments of the same slice are performed. The different coding in each experiment results in a volume selective signal if the four signals are subtracted as indicated.

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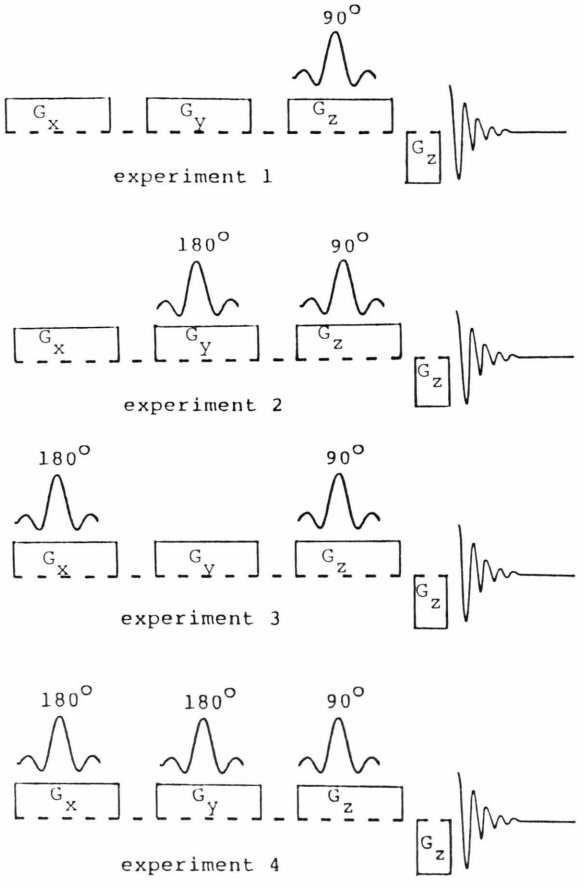

	$180°/G_x$	$180°/G_y$	$90°/G_z$	Receiver
Experiment 1			x	+
Experiment 2		y	x	−
Experiment 3	$-y$		x	−
Experiment 4	$-y$	y	x	+

Fig. 2. The sequences of the four CODEX experiments and their corresponding phasecycle. All gradients are switched in each of the experiments.

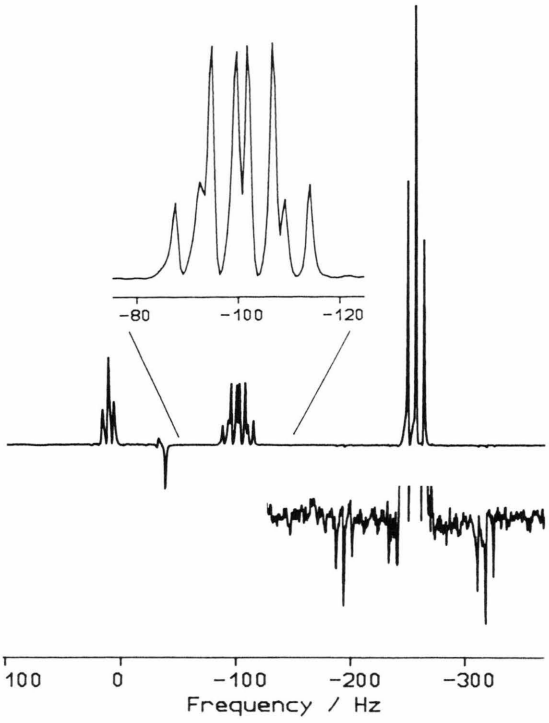

Fig. 3. Localized proton CODEX spectrum of a $(13\ \text{mm})^3$ cube of ethanol >95%. The high spectral resolution is demonstrated by the magnified part of the spectrum which shows the complex pattern of the methylene group. The ^{13}C satellites of the methyl group ($J_{C-H} \simeq 127$ Hz) are shown enhanced. The four signals were acquired and subtracted, the volume selective signal was Fourier transformed, phased, and baseline corrected. Experimental data: 4×16 acquisitions, TR = 15 s, T_2-sensitive time = 6 ms, dwelltime = 1 ms, $2k$ data points.

from which the acquired signal comes and the VOI is far smaller with the CODEX method. This effect results in a reduced sensitivity to subtraction errors and solves the dynamic problems of the ISIS method to a high degree. In addition, the size of the VOI can be reduced. Secondly, patient movement problems can be solved in several cases by the fact that the coded slice can be freely positioned and oriented. The advantages over the DRESS method are the property of CODEX to acquire a fully localized spectrum and the possibility to use any coil available for transmission and reception as well.

Experiments and Results

All experiments were carried out on a 1.5 T Siemens Magnetom whole-body imager operating at 63.6 MHz for protons and at 25.7 MHz for phosphorus. The pulses were 2.56 ms Hamming filtered sinc shaped pulses. The slice selection was performed with gradients of $2 \cdot 10^{-3}$ T/m. In all proton experiments the double spin echo PRESS sequence [3, 12, 17, 18] was used to shim on the VOI.

The application of CODEX to the protons of ethanol >95% is shown in Figure 3. For this experiment a cylinder 170 mm in diameter and 80 mm in height filled with doped water was placed with its symmetry axis perpendicular to the static field direction inside a Helmholtz coil (200 mm in diameter, 100 mm distance of the coil pair). The excitation was performed with the bodycoil. Inside the cylinder a

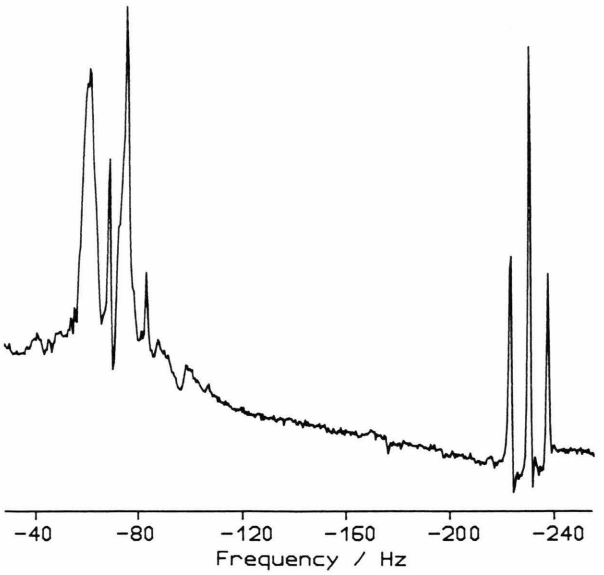

Fig. 4. Water suppressed localized proton CODEX spectrum of a $(13\ \text{mm})^3$ cube located within a bottle of "Alkoholfreies Bier" (nonalcoholic beer). Nevertheless ethanol signals of the methylprotons (-230 Hz) are clearly visible. The volume selective signal was Fourier transformed and phased, no further data manipulation was performed. Experimental data: 4×2 acquisitions, TR = 12 s, T_2-sensitive time = 6 ms, dwelltime = 1 ms, $2k$ data points.

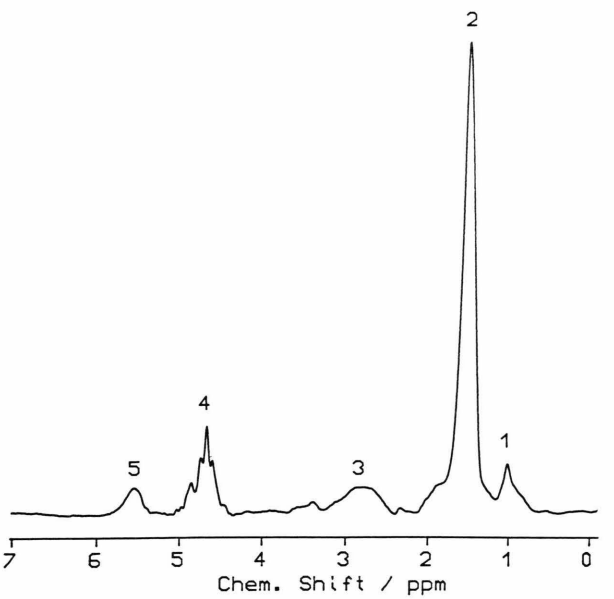

Fig. 5. *In vivo* localized CODEX proton spectrum. A $(13\ \text{mm})^3$ cube was positioned within the yellow bone marrow of the femur of a normal volunteer. The volume selective signal was Fourier transformed and phased, no further data manipulation was applied. This measurement was performed in cooperation with K. Küper, Department of Radiology, University of Tübingen. Experimental data: 4×4 acquisitions, TR = 12 s, T_2-sensitive time = 6 ms, dwelltime = 1 ms, $2k$ data points.

small bottle filled with ethanol >95% (30 mm diameter, 70 mm height) was placed. The proton spectrum in Fig. 3 shows the resonances of methyl- (-260 Hz), methylene- (-100 Hz) and hydroxylprotons (10 Hz). Due to the fact that the methyleneprotons are coupled to the methylprotons ($J_{H-H} \simeq 7.2$ Hz) and the hydroxyl protons ($J_{H-H} \simeq 5.4$ Hz) they show a complex multiplet structure with linesplittings smaller than 2 Hz. To demonstrate the spectral resolution, which is better than $2 \cdot 10^{-8}$, a magnified version of the methylene multiplet is also given in this figure. The stability of the magnet and the method as well are obviously very high. Therefore the linesplittings in this spectrum can be used for time stability investigations [20]. The transmitter frequency was adjusted to the water resonance of the whole phantom. It is represented by zero on the frequency scale. The quality of the spatial selection is very good since almost no water signal is visible at or around the transmitter frequency. The small inverted resonance at -35 Hz is the residual water signal of the ethanol sample, which is <5%. Since the T_2-sensitive time of this CODEX spectrum is 6 ms, only spurious phase anomalies due to the J couplings are visible in the multiplets. The sensitivity of the CODEX method can be derived from the ^{13}C satellites (see enhanced part of the spectrum in Fig. 3) which are 200 times less intensive than the main methyl signal.

The sensitivity of CODEX is also demonstrated in Fig. 4, which shows a water suppressed proton spectrum out of a 0.5 l bottle of commercially available "Alkoholfreies Bier" (nonalcoholic beer). In spite of this claim the volume selective spectrum of the beer shows a clearly detectable content of ethanol which is about 0.5%. In addition a few further broader signals are visible which obscure the quartet of the methyleneprotons of ethanol. These signals presumably stem from residual sugars. The water suppression in this spectrum is done by a frequency selective inversion (bandwidth 75 Hz) of the water resonance before each CODEX experiment.

One example of a human *in vivo* investigation is presented in Figure 5. This proton spectrum of yellow bone marrow of the femur of a normal volunteer is obtained with the coil for extremities which served for transmission and reception. The spectrum of a $(13\ \text{mm})^3$ cube shows a high resolution because the

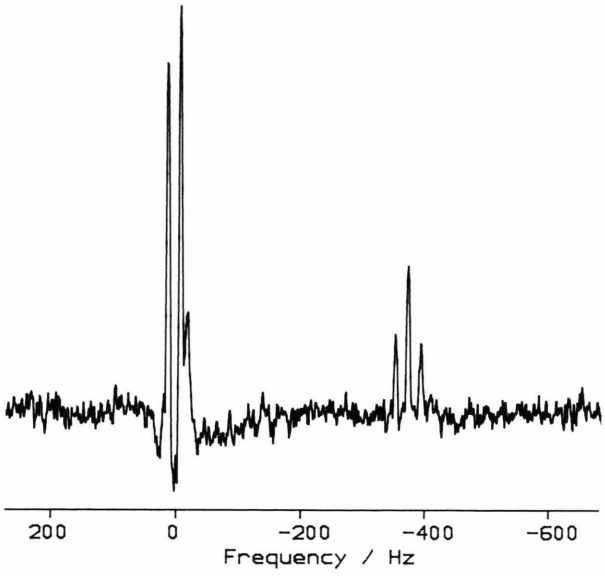

Fig. 6. Localized ^{31}P CODEX spectrum of a (62 mm)^3 cube of a 0.1 molal aqueous solution of $Na_5P_3O_{10}$. The volume selective signal was multiplied with an exponential function (half height at 100 ms), Fourier transformed, and phased, no further data manipulation was applied. Experimental data: 4×1 acquisition, T_2-sensitive time = 3 ms, dwelltime = 250 μs, 1 *k* data points.

methyl- (1) and methylenesignals (2) are completely resolved. Further signals are: $O{=}CH_2$ groups (3), water (4) and vinyl (5). The assignment was done following [21, 22].

Experiments with ^{31}P were performed using a headcoil for transmission and reception. Inside this coil a 1 l bottle filled with a 0.1 molal aqueous solution of sodium triphosphate ($Na_5P_3O_{10}$) was placed. No shimming procedure was carried out. The spectrum of Fig. 6 obtained with a volume of (62 mm)^3 with 4×1 acquisition shows a triplet at -380 Hz which stems from inner phosphorus nuclei of the molecule and a doublet at 0 Hz resulting from the two outer phosphorus nuclei. A small diphosphate impurity is also visible at -40 Hz. In spite of the homonuclear coupling of $J_{P-P} \simeq 19$ Hz the multiplets show almost no phase anomalies because the T_2-sensitive time is only 3 ms in this experiment.

CODEX is a subtraction method which combines the advantages of ISIS and DRESS. Due to its short T_2-sensitive time, spectra of ^{1}H and ^{31}P can be obtained with negligible distortions of *J* coupled signals and with a negligible T_2-weighting. The use of surface coils for reception and transmission as well is possible, the latter e.g. in combination with hyperbolic secans pulses [23]. The coded slice can be freely positioned and oriented so that movement problems which may occur *in vivo* can be solved in many cases. ^{1}H T_1-measurements and spectroscopic investigations with other nuclei, e.g. sodium, have been found to be possible with CODEX.

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