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Single potential analysis of cavernous electric activity (SPACE)—experiences and refinements

CHRISTIAN G. STIEF MD AND LUC MERCKX MD

Department of Urology, MHH, Hannover/Germany and Department of Urology, Academisch Ziekenhuis, Vrije Universiteit, Bruxelles/Belgium.

Recently, electromyography of the cavernous bodies was introduced by Wagner and Gerstenberg. The refinement of this methodology, the single potential analysis of cavernous electric activity (SPACE), seems to enable the diagnosis of cavernous smooth muscle myopathy and of cavernous autonomic neuropathy—all in analogy to the classical EMG of the striated muscle. SPACE was done in over 500 patients with erectile dysfunction and in 82 normal subjects. The low frequency cut off was set at 0.3, 0.5 or 2 Hz and the high frequency cut off at 32, 100, 500 or 2000 Hz. In normal men, SPACE showed a regular electrical activity with potentials of low frequency and electrical silence in between. The potentials were synchronous throughout the cavernous bodies. In patients with peripheral autonomic denervation, asynchronous potentials with higher frequency (up to 250 Hz) and irregular shape were found. Patients with upper spinal cord lesions often showed normal potentials together with abnormal potentials and whips. Surface electrodes resulted in recordings similar to needle electrodes. We conclude that cavernous electric activity can be recorded. Our results strongly suggest that SPACE is a reproducible diagnostic tool for erectile dysfunction.

Key words: cavernous smooth muscle, electric activity, diagnosis, autonomic neuropathy

INTRODUCTION

A refined diagnostic approach for evaluating erectile dysfunction was developed during the last decade. Today, the two mainstays—and the most widespread diagnostics—of the diagnosis of erectile dysfunction are under strong criticism: pharmacotesting largely depends on adequate cavernous smooth muscle relaxation that cannot be monitored without additional apparative help of SPACE (only used occasionally); Doppler, Duplex or colour Doppler of the penile arteries do not stand critical evaluation and we have increasing data that these methods often cannot discriminate between normal subjects and patients with erectile dysfunction ([1]; own unpublished results). Since the important role of the cavernous smooth muscles is

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Correspondence address: Christian G. Stief MD, Department of Urology, MHH, D-3000 Hannover 61/Germany.

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becoming more and more appreciated, the diagnosis of its cellular intactness and its state of autonomic nervous supply is crucial for an adequate treatment of our patients. Although Eckhard described and functionally examined the autonomic innervation of the cavernous bodies in 1863[2], a diagnostic method for the autonomic cavernous innervation was not available until recently. In 1988, Wagner and Gerstenberg were the first to describe the electrical activity of the cavernous tissue[3]. They described that a periodical electric activity disappears during flaccidity and postulated that a non-disappearance would be suggestive for cavernous autonomic dysfunction[4,5]. In 1990, a different data processing was described by us with an interpretation of the individual potentials of cavernous electric activity (SPACE), that possibly allows the diagnosis of cavernous autonomic dysfunction and smooth muscle degeneration during flaccidity[6].

In the following we would like to present our current methodology for registration of cavernous electric activity, our interpretation of the findings and its consequences for the diagnosis and treatment of erectile dysfunction.

Patients and methods

After basic evaluation and winning of the patient's confidence, SPACE evaluation is done in all patients with erectile dysfunction in a relaxed atmosphere. With the patient in the supine position with the trunk elevated at an angle of about 30° (this elevation results in better recording that we cannot explain), two needle electrodes are placed bilaterally in the proximal penile shaft: after appropriate disinfection, the needles are pierced in a right angle through the tunica albuginea, then pushed medio-proximally into the cavernous bodies for about 15 mm. The neutral electrode is placed on the anterior surface of the upper thigh.

Since needle electrodes give a better recording with 'sharper' potentials (in surface electrode recording, the skin filters out the high frequencies, resulting in 'rounder' potential shape with decreased amplitude that is more difficult to interpret), we are now using them in most patients. In case we use surface electrodes, the skin is meticulously cleaned and the electrodes then placed bilaterally over the proximal penile shaft. The close positioning of the surface electrodes over the cavernous bodies is very important, since minimal malpositioning will result in inappropriate recording.

The potentials are routinely processed by an electrophysiological unit (Spacerecorder, Wiest, Germany) with the cut off frequencies at 0.3 to 32 Hz and the paper speed at 0.5 cm/sec. For special indications, we are using more sophisticated research devices with wider frequency ranges and triggering facilities.

After placing the electrodes and connecting them to the Spacerecorder, the patient is advised to restrain from any movements to avoid artefacts during the recording. Furthermore, any movements by other persons than the patients are minimized since they may also interfere with the recording. To avoid false results by a high sympathetic tone of the patient (stress, performance anxiety, inappropriate preparation of the patient) or by the injury of the smooth muscle cells by the needle insertion, the examiner leaves the room for about 10 to 20 minutes and the patient can adapt to the situation. Then, recording is started (during flaccidity) for 30 to 40 minutes. We usually leave the room during the first 10 minutes of recording; we then re-enter the room, observe the patient simultaneously with the recording and go into details of his case history. Often, this mild intellectual work of the patient slightly elevates the sympathetic tone, thus increasing the frequency of potentials, rendering the interpretation easier.

Results

Normal subjects

In the normal man, cavernous electric activity shows a consistent pattern that is comparable to other smooth muscle cells, such as uterus, ureter, trachea or stomach[8]. During flaccidity, a high frequent basic electrical activity of low amplitude (less than 5 μV) is found. This basic activity may be wavelike due to myogenic activity. This basic activity is, in the usual amplification, recorded as thin, straight line or electrical silence; only higher amplification shows that this baseline activity is not complete electrical silence. This basic activity is interrupted by phases of strong electric activity, the 'potentials'. These potentials were very similar within the same patient over the period of the examination and were of great similarity in most of the normal men. Their duration is about five to 15 seconds and their shape recalls on mono-, bi- or triphasic action potentials of the striated EMG (although the smooth muscle potentials are much slower; Fig. 1). Simultaneous recording with needle electrodes in both cavernous bodies shows synchronization of the potentials within the whole cavernous bodies in the normal man (Fig. 2). This synchronization of the cavernous electric activity within the cavernous bodies results in a relatively big potential that can easily be picked up by surface electrodes when they are placed appropriately (Figs 1 and 3).

When done with surface electrodes, frequency analysis of the potentials in normal men showed the potentials to be mostly in a frequency range below 5 Hz. When the lower cut off frequency is set below 0.5 Hz (or even below 0.1 Hz), wavelike base-line activity becomes so preponderant that it markedly disturbs the interpretation of the recordings. However, abnormal cavernous electric activity (see below) often shows a much higher frequency range with activity found up to over 100 Hz. At present, we therefore use a frequency range from 0.3 to 32 Hz or from 0.5 to 100 Hz (depending on the recording device) for routine SPACE examination. Here, it is important that the printer is able to reproduce what the amplifier is able to record. Using this frequency range, the potentials in normal men have a mean duration of about 13 seconds, a mean amplitude of about 440 μV and a mean poliphasity of about 14.

When audiovisual sexual stimulation is applied to normal man, potentials show a uniform change in most patients: with increasing tumescence and rigidity, frequency of the potentials increased while the amplitude decreased, until high frequent potentials of low frequency were seen at full erection; often, full rigid erection is associated with an 'electrical silence' at the usual amplification. Nonetheless, when stress was applied during full erection, big potentials were seen although full erection was still maintained. This finding suggests that at the end of a physiologic erection, cavernous smooth muscle cells are being contracted although a full erection state is still maintained at this moment.

During pharmacologically induced full erections, cavernous electric activity is even more reduced than in physiologically induced erections.

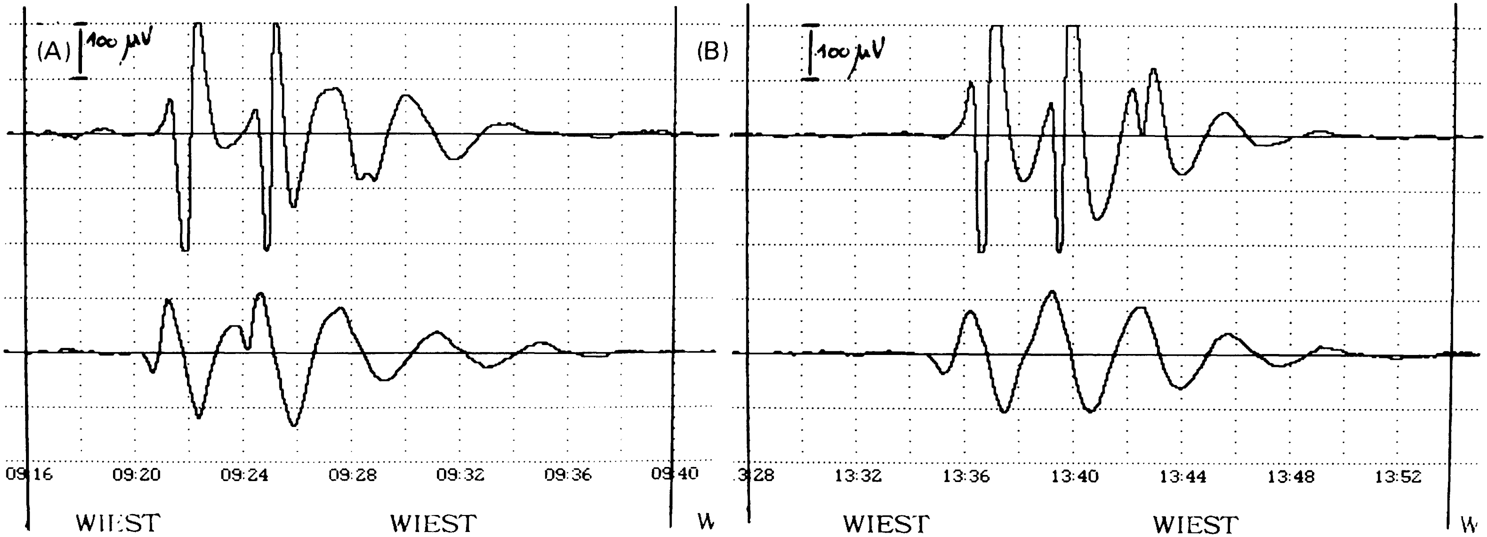


FIGURE 1. Simultaneous recording of cavernous electric activity with monopolar needle (upper tracing) and surface electrodes (lower tracing) electrodes shows similarity of these recordings with phases of electrical silence and phases of high electrical activity ('potentials'). (a) and (b) are typical potentials of the same individual.

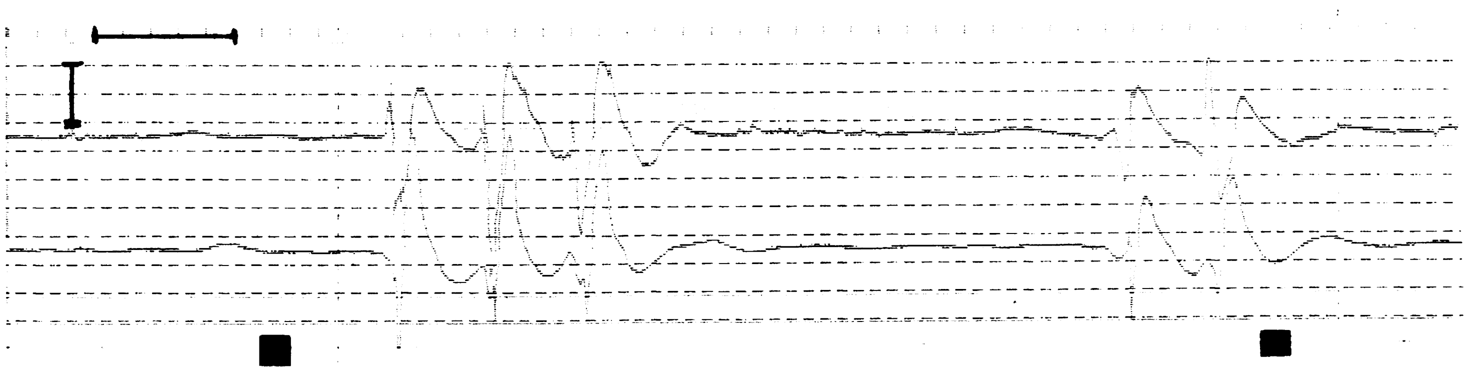
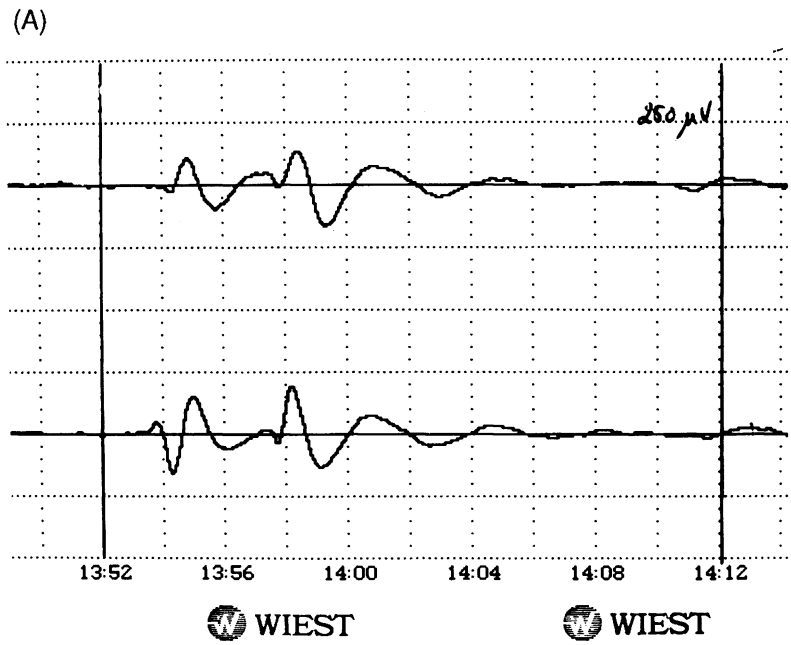


FIGURE 2. Recording with concentric needle electrodes in both cavernous bodies shows synchronization of cavernous electric activity (tri- and biphasic) in the normal subject. The horizontal bar is five seconds, the vertical 100 μV.



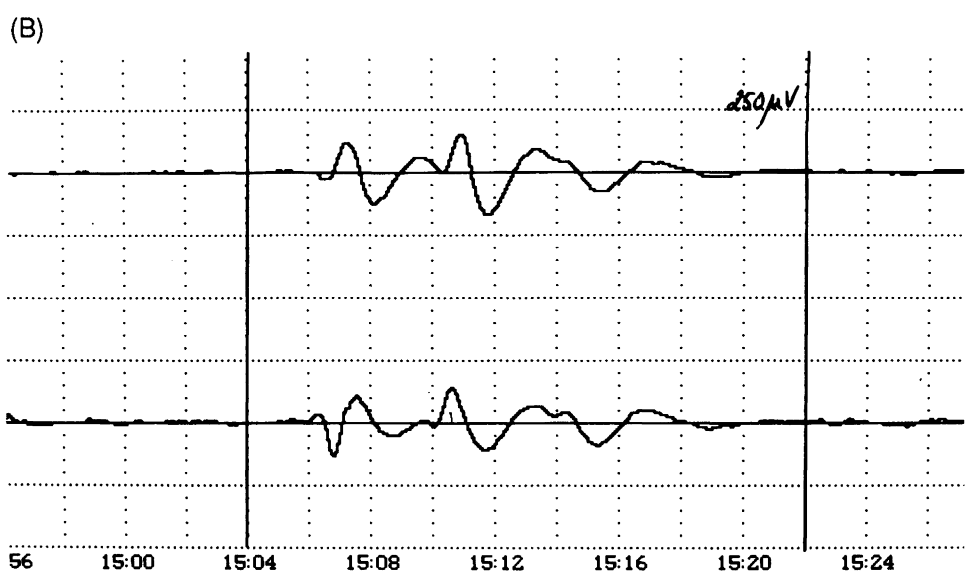


FIGURE 3. Recordings done with 2×2 surface electrodes bilaterally placed over the penile shaft. (a) and (b) are typical potentials of the same individual.

Patients with disruption of the peripheral autonomic supply

In patients after radical cystoprostatectomy, abdomino-perineal extirpation of the rectum or pelvic fracture with complete disruption of the urethra at the level of the urogenital diaphragm, peripheral cavernous autonomic supply is most likely disrupted. In these patients, small abnormal potentials of low amplitude, high frequency and irregular periodicity as well as whips (potentials with a fast convex phase of depolarization and a concave shape of repolarization; in the striated muscle, similar shaped potentials were found in denervated muscles) are found (Fig. 4). Cavernous electric activity is not synchronized in these patients.

In some of these patients and in most patients after nerve spearing radical prostatectomy (but impotence postoperatively), cavernous autonomic supply may have been partially spared. Here, normal and abnormal potentials are found and cavernous electric activity is sometimes synchronized, sometimes not (this coexistence of normal and abnormal electric activity suggest only a partial destruction of the autonomic cavernous supply; Fig. 5).

Lesion of the upper motor neuron

In most patients with complete spinal cord injury between the level of C7 and Th 12, cavernous electric activity often looked rather normal: we found potentials with a longer duration than in the normal (multiple action potentials); the amplitude was comparable to normal potentials, as well as the time of the passages between the zero line. Cavernous electric activity was synchronized for the above described potentials, but was not synchronized for whips and other abnormal potentials of lower amplitude and higher frequency (Fig. 6).

In most patients with a complete spinal cord lesion at a cervical level, no normal potentials with synchronization in both cavernous bodies were found. Here, SPACE recording showed high frequent, irregular cavernous activity, mostly without well-defined (yet abnormal) potentials and without electrical synchronization of the cavernous bodies. Only few patients showed a silent electrical base line with most patients presenting a permanent irregular, high frequent electric activity (Fig. 7).

Patients with cavernous smooth muscle degeneration

In many patients with long lasting insulin-dependent diabetes (over 20 years), clinical evaluation suggested cavernous smooth muscle degeneration: they had a poor response to intracavernous injection of vasoactive drugs and showed extensive venous leakage in pharmaco-cavernosometry.

In these patients, SPACE showed irregular potentials with low amplitude and slow depolarization speed. Synchronization of these abnormal potentials was occasionally found (Fig. 8).

Discussion

Many studies show that the electric activity of cavernous smooth muscles can be recorded (3, 4, 10 presentations at the 5th World Meeting on Impotence, Milan 1992). The reproducible recordings and the similarity of the potentials in normal patients

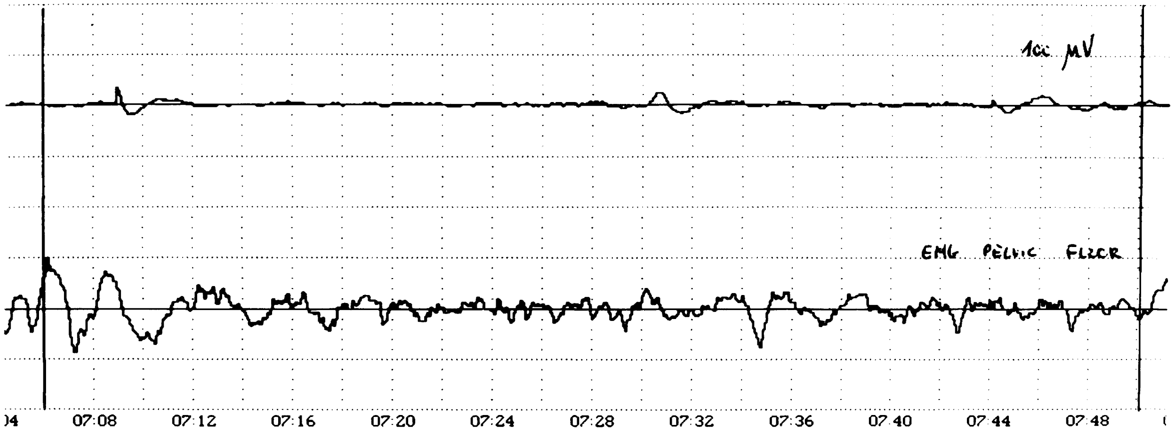


FIGURE 4. After radical cystoprostatectomy, no regular potentials are found; there is no synchronized cavernous electric activity in both cavernous bodies. The upper tracing is SPACE, the lower pelvic floor.

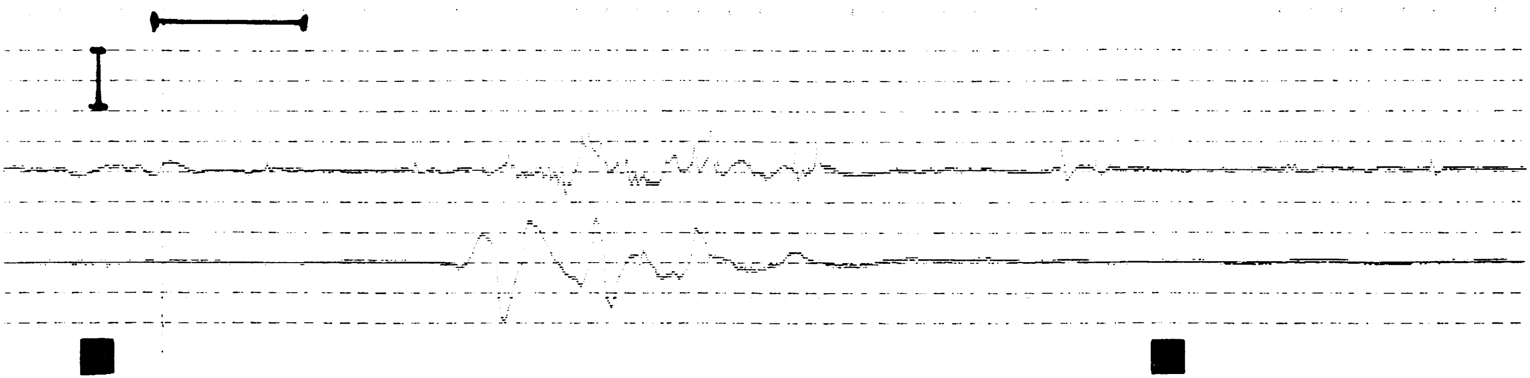


FIGURE 5. After radical prostatectomy, abnormal (upper tracing) and normal (lower tracing) recordings were observed. The horizontal bar is five seconds, the vertical 100 μV.

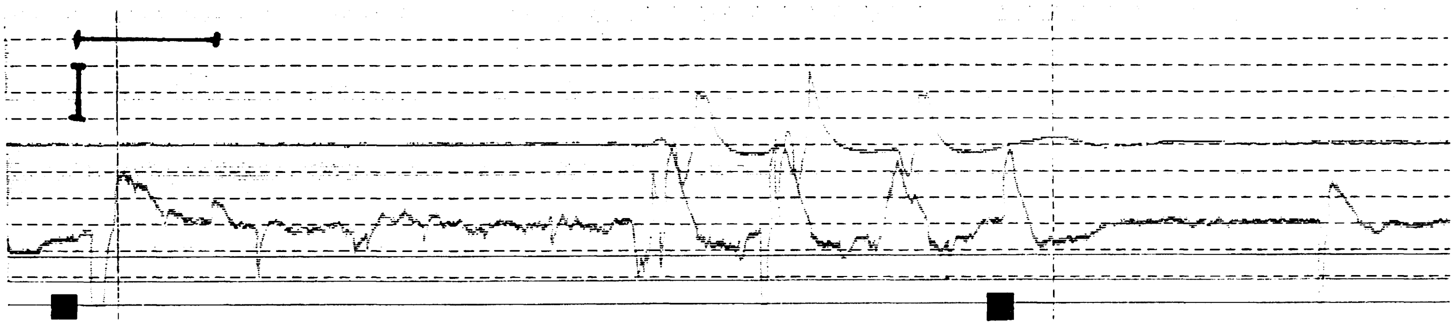


FIGURE 6. In a patient with complete spinal cord injury at Th 12, SPACE showed potentials of similar amplitude to the normal with asynchronous whips. The horizontal bar is five seconds, the vertical 100 μV.

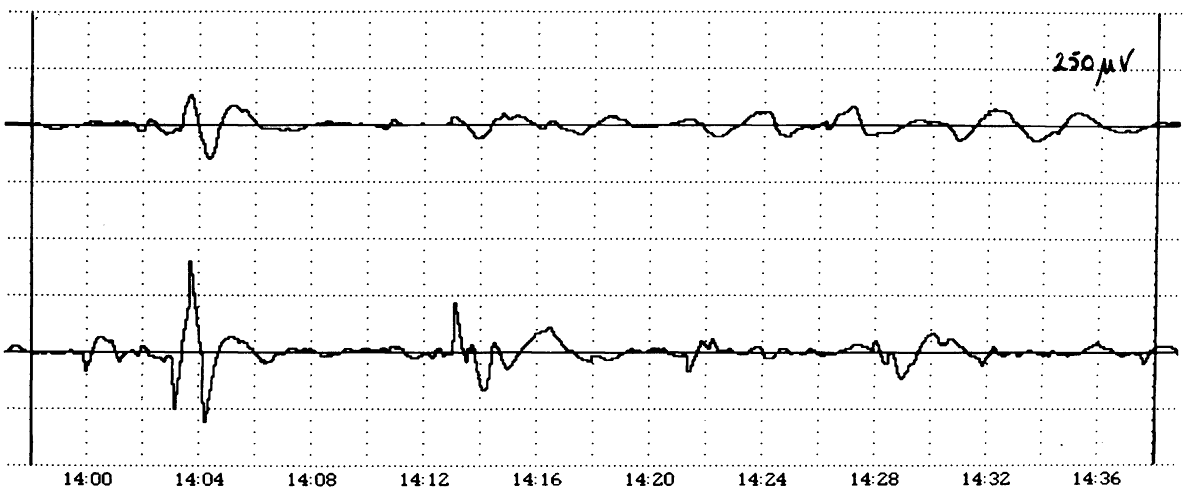


FIGURE 7. In a patient with a C6 lesion, high and low amplitude, higher frequency potentials with and without synchronization are found with needle electrodes.

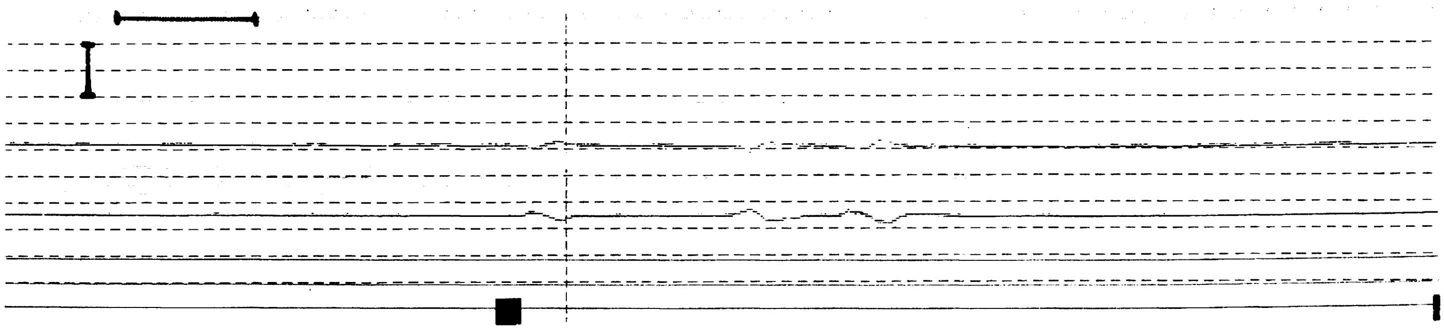


FIGURE 8. In this diabetic patient with an onset of over 25 years, SPACE shows a low amplitude electrical activity with slow depolarization speed of the potentials. The horizontal bar is five seconds, the vertical 100 μV.

as well as the different recordings during full erection to AVSS on one hand and to intracavernous injection of vasoactive drugs on the other strongly suggest that the recordings are not artefacts. The similarity of the potentials recorded with intracavernous needle electrodes and with surface electrodes on the penile skin suggest that the potentials are of electrical and not of myogenic (movement) origin. This is supported by the extracellular recording of cavernous electric activity in isolated muscle strips. The potentials recorded in normal patients are similar to smooth muscle potentials recorded in other smooth muscle organs in human or other species, as in uteral, tracheal or gastric smooth muscles[7,8,9].

Our findings in normal patients suggest that during flaccidity, the contractions of the cavernous smooth muscle cells are synchronized by the sympathetic tone in a periodical rhythm that is influenced by the psychogenic relaxation of the patient. This results in longer phases (30 to some 100 seconds) of electrical silence; here, cavernous smooth muscle cells contract non-synchronously, resulting in an electrical activity of low amplitude (less 5 μV) and high frequency—at the usual amplification, an 'electrical silence'. These phases of electrical silence are interrupted by phases of (presumably sympathetically mediated) synchronized electrical activity, the potentials. Here, a potential of high amplitude (up to 1 mV) and long duration (up to 15 seconds) can be simultaneously recorded in different areas of both cavernous bodies.

One of the anatomical bases for these electrophysiological findings is the detection of GAP junctions between human cavernous smooth muscle cells by Moreno and co-workers[10]. During sexual arousal and with increasing tumescence and rigidity, the sympathetic tone is dramatically reduced and parasympathetic neurotransmitters are released, resulting in a relaxation of the cavernous smooth muscle cells. This relaxation impulse is transmitted via the gap junctions to other cells. This results in a complete relaxation of all cavernous smooth muscle cells; electrically, we see potentials of decreased amplitude and length, with an increase in frequency during flaccidity, until electrical silence is reached during full rigid erection.

An abnormal cavernous electric activity may be due to an abnormal cavernous autonomic supply or to abnormal cavernous smooth muscle cells, or to both factors. In case of a disrupted peripheral autonomic supply, it may be that groups cavernous smooth muscle cells (within these groups, smooth muscle cells are synchronized by the gap junctions) are now not synchronized by the central input, resulting in abnormal, non-synchronous potentials. It may also be that disruption of the central input leads to a cavernous smooth muscle degeneration[11] with a loss of gap junctions. Again, SPACE will record abnormal, non-synchronous potentials.

In patients with a complete spinal cord injury between the levels of C7 and S1, an autonomic sacral parasympathetic innervation with a partially intact central sympathetic innervation is found. This may be responsible for the longlasting potentials with a silent electrical base line. In most patients with cervical lesions, no specific potentials and no silent electrical baseline was found; these recordings may be caused by complete central sympathetic and parasympathetic denervation with simultaneous activation of the sympathetic and parasympathetic spinal centres.

In patients with cavernous smooth muscle degeneration, cavernous electric activity seems to be directly due to the cell degeneration; influences of a possible autonomic dysfunction could not be ruled out in this series and are of minor practical importance.

Recently, the postoperative outcome after at least a six-month follow up of penile venous surgery has been evaluated in our department. There has been no significant correlation between the preoperative diagnostics (age, risk factors, Doppler, maintenance flow) and the postoperative outcome except the SPACE results (44 patients in total): out of the 20 patients with normal SPACE, 12 had full erections postoperatively, four failed and four responded to pharmacotherapy. Of the 26 patients with abnormal SPACE, one developed a full erection, one responded to pharmacotherapy and 24 failed. Should this trend be confirmed by larger numbers, the indication for penile reconstructive surgery versus penile prosthesis could be dramatically improved.

In our departments, SPACE has become (with pharmacotesting) the basic evaluation of patients with erectile dysfunction. Nonetheless, a refined recording device for broader availability is urgently needed to further elaborate the method's potential. Furthermore, standardization of recording (monopolar/concentric/surface electrode; frequency range; flaccidity/visual stimulation/pharmacostimulation) and interpretation is necessary; to join forces for these projects, we will therefore organize a consensus meeting on cavernous EMG/SPACE to be held 16–18 April 1993.

References

1 Meuleman EJH, Belemans BLH, Doesburg WH, Asten WNJC, Skotnicki SH, Debruyne FMJ. Penile pharmacological duplex ultrasonography: a dose effect study comparing papaverine, papaverine/phentolamine and prostaglandine E1. J Urol 1992; 148: 63–68.

2 Eckhard C. Untersuchungen über die Erektion des Hundes. Beitr Anat Physiol 1863; 3: 123–146.

3 Wagner G, Gerstenberg T. Human *in vivo* studies of electrical activity of corpus cavernosum. J Urol 1988; 139: 327A.

4 Gerstenberg TC, Nordling J, Hald H, Wagner G. Standardized evaluation of erectile dysfunction in 95 consecutive patients. J Urol 1989; 141: 857–862.

5 Wagner G, Gerstenberg T, Levin RJ. Electrical activity of corpus cavernosum during flaccidity and erection of the human penis. J Urol 1989; 142: 723–729.

6 Stief CG, Djamilian M, Schaebsdau F, Truss M, Schlick R, Abicht J, Allhoff EP, Jonas U. Single potential analysis of cavernous electric activity. World J Urol 1990; 8: 75–82.

7 Wagner G. Contractility of myometrial transplants. In: Physiology and genetics of reproduction, part B, ed. by Coutinhu EM and Fuchs F. Plenum, New York, 1976.

8 Couturier D. Gastric electromyography. In: Clinical investigation of gastric function, ed. by Scarpignato, C., Bianchi, PG. Fron Gastrointest Res 1990; 17: 297–314

9 Kondo T, Tamura K, Onoe K, Takahira H, Ohta Y, Yamabayashi H. In vivo recording of electrical activity of canine tracheal smooth muscle. Am Physiol 1992; 72(1): 135–144.

10 Moreno AP, Campos AC, Christ GJ, Melman A, Herzberg EL, Spray DC. GAP junctions between human corpus cavernosum smooth muscle cells in primary culture: electrophysiological and biochemical characteristics. Int J Impotence Res 1990; 2 (Suppl 2): 55–57.

11 Paick JS, Göldsmith PC, Barta AK, Nunes L, Padula CA, Lue TF. Relationship between venous incompetence and cavernous nerve injury: ultrastructural alteration of cavernous smooth muscle in the neurotomized dog. Int J Impotence Res 1991; 3: 185–192