Concept of system allowing non invasive detection of uterine contractions in women undergoing In Vitro Fertilization – Embryo Transfer treatment

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Abstract. Uterine contractile activity in women undergoing advanced fertility treatments such as IVF-ET (In Vitro Fertilization – Embryo Transfer) might constitute one of the factors influencing embryo implantation rates, and by that – the success rates of the treatment. In early 1990's it was confirmed that IVF-ET patients experiencing active uterine contractions had up to 3-fold lower success rates as compared to the ones with silent uteri. However, even though it occurs in about one third of patients, exaggerated uterine contractions are not a subject of routine diagnostic tests or any treatment. One of the reasons for that is the lack of appropriate, reliable tools allowing identification of such patients. This paper presents a system enabling easy, non invasive identification of uterine contractions in non pregnant women. Application of the method described in this publication could be helpful in identifying IVF-ET patients with active uterine contractions, who could benefit from additional treatment which could potentially increase their chances for conceiving.

Introduction

Detection, recognition and analysis of signals is inadvertent part of biomedical research projects using multimedia data types such as images, film or sound sequences. In general, the process of signal analysis starts from acquiring appropriate data at the time of patients' examination. Subsequently, following the analog to digital conversion, data is placed in a specially designed framework, for instance a multimedia database.

Digitally recorded signals can be reviewed whenever needed, however, further analysis requires extraction of information which could be presented in quantitative measures, such as length, width, volume or changes of object's shape in time. Analysis of film sequences is relatively complicated as it comprises of both image analysis and the analysis of temporal changes

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of such. One of the basic methods applied in analysis of film sequences are analysis of separate film frames with subsequent string analysis of results. Another method focuses on temporal analysis of specific structure of an image. When analyzing film sequences with unstable position of a region of interest, a specific correction against the stable benchmarks needs to be used.

Our paper is presenting a method of analysis of ultrasound image of non pregnant human uteri allowing identification of the contractile activity. The analysis procedure comprises of several stages – namely – setting an observed section of an image, generation of a graph of temporal changes of image parameters and detection of a region of uterus which is the most indicative for uterine contractions (it is the so called endometrial interface). The current method's novelty is an ability of an automatic identification of the endometrial interface. None of the previously published reports enabled the above which was potentially a source of bias [2, 4].

Significance of uterine contractile activity in fertility treatments

Uterine contractile activity is an important component of its receptivity, affecting the process of implantation of embryos [15]. Uterine peristalsis was found to be much higher in the IVF-ET cycles than in the natural ones [16]. Uterine contractions are negatively correlated to the implantation rates in women undergoing embryo transfer, a final stage of IVF–ET treatment [2]. Notwithstanding that increased uterine contractions are found in one third of IVF-ET patients, elevated uterine contractile activity is currently not a subject of any routine diagnosis or treatment [1].

Uterine contractions can be objectively measured by placing the intrauterine pressure transducer and recording the pressure changes [3]. Such an approach is however not acceptable in patients who are about to have Embryo Transfer procedure as it is related to endometrial trauma which severely decreases the chances for successful embryo implantation.

Consequently, non invasive methods of detection and analysis of uterine contractions should be applied. Ultrasound scan is the easiest non invasive method of collection of images of uteri. Within the uterus, one can describe two most distinctive layers – myometrium (outer, hypoechogenic) and endometrium (inner, hyperechogenic). The border between the two is called junctional zone [5]. Changes in junctional zone are reflective of uterine contractions [4–5].

Analysis of ultrasound scans of non pregnant uteri has been a subject

of a number of reports which focus rather on the observer counting uterine contractions or analysis of very local (single point) changes of endometrial interface [1–2, 4]. More global approach allowing multi-point analysis of uterine peristalsis could allow not only detection but also determination of direction and power of contractions. Apart from being an interesting clinical research tool, such a method could be more adequate in the identification of women in risk of unsuccessful embryo implantation. It could increase their chances for successful treatment which is especially important in groups with poorer prognosis such as women of above 40 years old age group [10].

Application for automatic detection of uterine contractions

The ultrasound scans of non pregnant uterus have been performed on consented patients of the Department of Reproduction and Gynaecological Endocrinology, Medical University of Bialystok, being prepared for the Embryo Transfer procedure (a final step of IVF-ET). For the scans, the GE Voluson Expert 730 scan system equipped with Sony VRD–MC6 recorder was used. Film sequences have been stored on DVD disks and converted to AVI format for further usage.

The very first stage of the project was the preparation of a purpose built application for the analysis of ultrasound scan images named Scan Studio. It has been created in Delphi based programming environment with the use of Embarcadero RAD Studio XE2 package.

Upon opening, the Scan Studio application allows uploading the AVI file with ultrasound scan recording and displays its very first frame. Subsequently, with a use of side scrollbars it is possible to position user defined gate identifying the transsection along which the image analysis is going to be performed. The coordinates of the gate's endpoints are displayed and can be used for exact replication of an analysis if needed. The properly adjusted gate is perpendicular to the long axis of the uterine body and is symmetrically covering the transsection of an endometrium and adjacent margin of myometrium [Fig. 1]. This stage is dependant on the user, however, it is relatively simple and it is unexpected that it might be a source of a significant bias.

When the AVI file is played, the Scan Studio automatically detects endometrial interface by using two alternative, user defined methods – means of neighbourhoods or medians of neighbourhoods. The result of the detection is displayed on a time axis in a lower part of the screen, below the

image of the uterus [Fig. 1]. For improved visualization, the length of time axis is fixed and equal to the referred screen section. It allows constant inspection of the whole signal (no additional scrolling is required to review the resulting image).

Fig. 1. Upper section of the figure – optimal setting of the gate on the uterine sagittal cross section. Lower section – image resulting from automatic detection of endometrial interface (marked by bright lines)

The changes of pixels alongside the used defined gate (region of interest) are displayed below the image of an uterus. The analysis and automatic detection of the endometrial interface – lower section of [Fig. 1] – stops when the last frame of an AVI file is reached or it can be halted by user anytime, and the resulting JPG file is recorded.

Algorithms of detection of endometrial interface

Detection of endometrial interface is a key stage of operation of Scan Studio. As endometrium is distinctively more echogenic (brighter) as compared to surrounding myometrium, the application focuses on assignment of borders between darker and brighter regions within user defined cross section (the gate). The border between the endometrium and myometrium is not always explicit as there might be more echogenic (brighter) areas in

the myometrium or less echogenic (darker) areas within the endometrium. When the scan image of uterus is observed from a distance, endometrial interface is easily identified, however, when zooming in, one can find that the border is not unequivocal and that the image is noisy in that region.

One of the methods for detection of such a border is averaging of the signal according to the surrounding of each reference points, which is reducing minor deviations and results in finding the value which is dominant in the examined region. In Scan Studio two such methods are implemented which are based on the calculation of means and medians of neighbourhoods. The former (means of neighbourhood method) calculates the mean values in the neighbourhood of a given point alongside the chosen transsection. Subsequently, the application calculates maximal and minimal values for the whole transsection in each separate timepoint. It is assumed that the brightest point of endometrium is located within the uterine cavity and the position of the darkest points are set down separately for upper and lower endometrial interface. Basing on the distance between the marginal brightness values, the cut off point is determined, which represents the border between the endometrium and myometrium – an endometrial interface.

The alternative algorithm is constructed similarly to the described above, and it uses median values instead of means. Both algorithms produce similar results, though the means of neighbourhood method seems to be more exact [Fig. 2]. The weakness of both is that in noisy images the detection of endometrial interface might be biased and might result in sudden shift in the detected endometrial interface occurring in the timepoint of images of poorer quality.

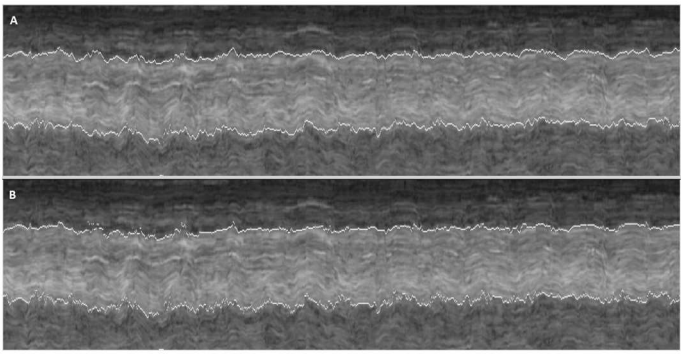

Fig. 2. Uterine contraction graphs produced by application of A – algorithm basing on means of neighbourhoods method, B – algorithm basing on medians of neighbourhoods method

Possibly more effective algorithm for the detection of endometrial interface could be employing the analysis of gradient of signal, when endometrial interface would be set in place of maximal increase or decrease of signal. It could be also associated with setting the medians or means in the surroundings which could – to some extent – eliminate the minor noise.

Another, also interesting approach, which might give even more adequate results could be applying the approximation of a value of the signal alongside the transsection of a sum of logistic functions. In such a case, the cutoff point could be determined in the point of extreme values of derivative functions of both logistic curves (maximum for increasing curve and minimum for decreasing one). It seems that in this approach the system could be more noise resistant.

Conclusions and future plans

Scan Studio provides an easy tool for delineating uterine contractile activity. Unique entity of the application is automatic detection of endometrial interface which is very helpful in detecting the uterine contractions. In its current form, the application can be used for detection of the frequency of uterine contractions and can identify the IVF-ET patients with elevated uterine contractility. Such patients contractions could be effectively treated with medications from the oxytocin antagonists group such as atosiban, which was shown to decrease contractions and promote embryo implantation [12, 14–15].

Further stages of development of the application involve implementation of additional algorithms for the detection of endometrial interface. Subsequent to that, we plan to incorporate the automation of detection of uterine contractions allowing the determination of their frequency and strength. Advanced data analysis could be used to determine the direction of contractions [13].

The completed and operational application can be incorporated within existing system of electronic registration of information about patients treated for infertility using IVF ICSI/ET method [7] with the statistical module [11] and the predictive module, based on the technology of artificial neural networks [6]. The whole system can be also merged with modules based on other advanced data-mining methods for analysis of IVF patients data [8–9].

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