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Computer Model of Gastric Electrical Stimulation

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Abstract—The aim of the study was to simulate gastric electrical stimulation using a computer model of gastric electrical activity and suggest a possible avenue toward reliable gastric pacing. Modeling was based on the conoidal dipole model of gastric electrical activity described earlier. It was assumed that local, nonpropagated contractions can be produced circumferentially using 4 rings of stimulating electrodes supplied with 2-sec phase-locked bipolar trains of 50 Hz, 15 V (peak to peak) rectangular voltage. Temporal and propagation organizations of gastric electrical activity described in the conoidal dipole model were used to derive the geometry of the stimulating electrodes and the time shifts for phase-locking of the electrical stimuli applied to the different circumferential electrode sets. The major assumptions and findings of the model were tested on two unconscious dogs. The model produced completely controllable simulated gastric contractions that could be propagated distally by phase-locking the stimulating voltage. The values of interelectrode distances in different rings, as well as the distances between the successive rings, were also derived. The concept of invoked circumferential contractions that are artificially propagated by phase-locking the stimulating voltage could be an avenue toward reliable gastric pacing of gastroparetic patients.

Keywords—Gastric electrical activity, Computer modeling, Gastric pacemaker, Gastroparesis.

INTRODUCTION

Gastric electrical stimulation has been a subject of research investigation for many years (1–5,9). The major reason to stimulate the stomach is the condition known as gastroparesis—the stomach is unable to grind, mix, and transmit the food to the duodenum and, in most cases, gastric emptying time is abnormally delayed (1,3). Many different ways to stimulate the gastric function were explored, including pharmacological, neural, purely electrical, and combined methods (1–5,9). Although some optimistic reports have been made (1,5) we believe that there are at least two questions about gastric stimulation that demand answers: (a) What kind of "*in vivo*" stimulation is being conducted with given parameters of the stimulating voltage or current—neural or direct smooth muscle stimulation? (b) When does stimulation invoke propagated contractions and when does it produce only local contractions?

In this study, we suggest a new approach in gastric electrical stimulation based on the conoidal computer model of gastric electrical field (6). The aims of the study were to: (a) develop the concept of gastric electrical stimulation using circumferential electrode sets and phase-locked stimuli derived from the conoidal model of gastric electrical field; (b) determine the geometry of the stimulating electrodes and the phase shifts between the stimuli applied to the different circumferential electrode sets; and (c) test the concepts and findings suggested by the computer simulation on two unconscious dogs.

METHOD

Modeling of Gastric Electrical Field and the Problem of Gastric Electrical Stimulation

Our recent study (6) suggested the conoidal dipole model of gastric electrical field. In this model, the area S of a δ-wide ring of depolarized cells represented as dipoles pointing toward the center was given with:

$$S = 2\pi\delta r(t), \tag{1}$$

where $r(t)$ represented the radii of the circles that built up this ring of dipoles. On the other hand, the relationship between the vector of the dipole density $\mathbf{D}$ and the vector of the equivalent dipole moment $\mathbf{P}$ (which is directly related to the number of depolarized cells in the ring and their depolarization level) is given with:

$$\mathbf{D} = \mathbf{P}/S. \tag{2}$$

Mirrizzi *et al.* (7,8) suggested that $|\mathbf{P}|$ could be considered constant and estimated its value to be 2.2×10^{-6} C · m. They assumed that the charge distribution on each side of a given polarized cell in the ring is approximately equal; and the number of polarized cells in the ring remains the same, whereas the density of the cells increases in distal direction with the decrement of S. In our present evaluations, we would deviate from this assumption and would consider $|\mathbf{P}|$ to be a variable. In fact, we would like to believe that changes in gastric electrical activity (GEA) associated with contractions cause the amplitude of this

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vector to fluctuate. However, these fluctuations could very well be obscured when the vector distance ρ between the point of interest and the infinitesimal area segment dS located on the ring of depolarized cells is sufficiently great (*e.g.,* in electrogastrography):

$$V_Q = [1/4\pi\epsilon] \int_{(S)} [\mathbf{D} \cdot \rho/|\rho|^3] dS. \quad (3)$$

The conoidal dipole model (6) and Eq. 3 relate to the spontaneous GEA of a normal stomach. Let us now consider the following possible problems related to the eventual abnormalities associated with the occurrence and propagation of the depolarization ring. Note that these abnormalities are strongly related to abnormal gastric function: (a) the ring of depolarized cells in a dysfunctional stomach might not have the same characteristics as the one observed in healthy subjects; (b) the propagation of the ring in distal direction might be disturbed; and (c) more than one depolarization ring might exist at the same time on the stomach wall.

Problem (a) simply indicates that the vector **P** in our conoidal dipole model of a dysfunctional stomach would not have the same value and possibly the same direction as the **P**-vector associated with normal stomachs.

Problem (b) implies that the mathematical expression describing the propagation of the ring in the conoidal model (6) is no longer valid and should be substituted with a different one to define the new pathological behavior of the stomach.

Problem (c) is related to the phenomenon of gastric electrical uncoupling and indicates that the stomach can be split into several different areas. In each of these areas, there is a separate ring of depolarized cells that has its own vector **P** and law of propagation.

Stimulation might be required when each of the above problems exists separately, or any combination of these problems is present. However, it is difficult, if not impossible, to separate quantitatively the problems and determine their relative significance in a given pathological situation. It could be assumed, though, that in most cases a stomach that would need pacing would be gastroparetic (*i.e.,* its spontaneous mechanical activity would be minimal or nonexistent).

It is well known (9) that gastric contractions are controlled by GEA. Moreover, when contractions are present, their temporal and propagation organizations are strongly related to the organization of GEA. Therefore, we should be able to reconstruct the temporal and propagation organizations of the missing contractions in a gastroparetic stomach using the existing model of gastric electric field, thus deriving a computer model of gastric electrical stimulation. With this model, we would: (a) explore the idea of artificially produced local circumferential contractions; (b) calculate the positions and determine the configurations of the circumferential electrode sets needed to produce these contractions; and (c) determine the exact delays between the phase-locked stimuli applied to these electrode sets so that a distally moving peristalsis is recreated.

Recreating the Temporal and Propagation Organizations of Gastric Contractions

Ideally, to empty a gastroparetic stomach, we should be able to recreate the temporal and propagation organizations of gastric contractions common for average healthy people. In this study, we suggest that this can be done by invoking local circumferential contractions and artificially propagating them toward the pylorus. The most important issues that demand answers are: (a) What is the geometry of the stimulating electrodes that can be used to produce a local circumferential contraction? (b) What is the frequency and duration of the stimulating voltage that would produce such contraction? (c) How do we phase-lock the applied stimulating voltages so that local circumferential contractions could be propagated from one electrode set to the next? (d) Are we stimulating the local nerves or the smooth muscles directly?

To address the first three of the above points, the following assumptions were made:

a. Regardless of whether the simulated stomach (a truncated conoid in spherical system of coordinates) (6) is able to produce an adequate ring of depolarized cells or not, and regardless of whether and how this ring moves distally, there are no contractions taking place in the stomach (*i.e.,* there is a complete gastroparesis and the organization and propagation of gastric contractions need to be recreated).
b. With an implanted serosal electrode pair (active and reference electrode positioned circumferentially at 3 to 4 cm apart) delivering stimulating bipolar rectangular voltage with defined frequency of repetition (50 Hz, peak-to-peak amplitude: 10 to 20 V) and duration (2 to 4 sec), it is possible to produce local (between, and slightly beyond the two electrodes) circumferential contraction that would last for the duration of stimulation.
c. The local contraction produced between the active and the reference electrode of a given electrode pair would displace the stomach wall toward the stomach axis by ~1 to 3 cm (depending on the amplitude of the stimulus) and would not propagate distally.
d. Phasic contractions take place simultaneously in circumferential planes (6–8).
e. Phasic contractions propagate with an increasing velocity toward the pylorus and have well-known temporal organization (6–8).
f. Only one circumferential contraction is present in the stomach at any given moment.

g. Only antral contractions are important from a mechanical point of view.

In our conoidal computer model (6), we assumed that the velocity of propagation (in centimeters/second) of the depolarization wave along the stomach axis of an average human can be expressed with:

$$v(t) = 0.00825 - 0.00575[\exp(-0.362t)], \qquad (4)$$

where $t = 0, 1, 2, \ldots, 19$ represents the discrete time (in seconds) for which the depolarized ring propagates from its origin in the midcorpus to the pylorus. The model considered the differences in the velocities of propagation along the greater and lesser curvatures as well. To incorporate these concepts into our stimulation modeling, we made the following additional assumptions:

a. The propagation of the band of depolarization takes place from the midcorpus (second No. 0) toward the pylorus (second No. 19) with an increasing and known velocity (6).
b. The time is discrete from 0 sec (the origin of the depolarization wave in the midcorpus) (6) to 19 sec (distal pylorus), with a step of 1 sec.
c. The first set of stimulating electrodes is placed in the proximal antrum at a position reached by the propagating depolarization band (described in the original conoidal model) (6) at second No. 7.
d. Each subsequent set of stimulating electrodes is located at a position corresponding to a 4-sec shift (the maximal allowed duration of the stimulation train), with respect to the previous one.

The exact distance of the circumferential electrode sets from the initial position of the depolarization ring in the midcorpus can be estimated from the exponential Eq. 4 for the velocity of propagation in an average human stomach (6):

$$1 = \Sigma_t\{[v(t) + v(t+1)]/2\} \cdot T; \qquad t = 0, 1, 2, \ldots, T_e - 1, \qquad (5)$$

where T_e is the second associated with the given electrode position and $T = 1$ sec.

The circumference of a given circle on which an electrode set was positioned was determined by the radius of that circle. This radius, which could be regarded as a function of the discrete time, was calculated using previously described technique (6). The number of electrodes in a given set could be calculated easily knowing the circumference and assuming that the interelectrode distance should be between 3 and 4 cm.

Testing the Model

One of the most important assumptions of the suggested method is that it is possible to produce local circumferential contractions when applying high-frequency bipolar stimulating voltage. This hypothesis was explored on two unconscious dogs. Two stainless-steel wire electrodes (one active and the other reference) were positioned 3 to 4 cm apart circumferentially (the electrode axis was perpendicular to the stomach axis) at different locations of the serosal side of gastric antrum. The effect of different stimulating bipolar rectangular voltages on the smooth muscle was examined. The frequency range of the stimulating voltage was 0.005 to 500 Hz, changed with a step of 10 times (*e.g.,* 0.005 Hz, 0.05 Hz, 0.5 Hz, etc). Furthermore, 3.0 ml of atropine was administered intravenously to block the cholinergic nerves and to determine whether the smooth muscle was stimulated directly, or the invoked contraction was a result from stimulating the cholinergic pathways.

RESULTS

Determining the Geometry of Stimulating Electrodes and Phase-locking the Stimuli

A net of circumferential stimulating electrodes was built up on the truncated conoid representing the stomach (6). All active electrodes and all reference electrodes in a given circumferential setup were separately "short-circuited" (*i.e.,* the active electrodes simultaneously delivered one and the same stimulation voltage, while the reference electrodes were attached to one and the same ground). Four separate circumferential setups—each having 6, 5, 4, and 3 electrodes, respectively—were used. The first ring of stimulating electrodes was positioned 4.3 cm distally from the midcorpus. Table 1 shows the distances between the circumferential electrode sets calculated from the central line between the greater and the lesser curvatures. These distances were calculated using Eqs. 4 and 5. In an actual setup, the arrangement of the electrode sets should probably start from the most distal set (Electrode Set No. 4, the closest to the pylorus), because the area of the midcorpus is not very clearly defined anatomically.

TABLE 1. Distances between different circumferential electrode sets estimated on the central line between the greater and the lesser curvatures on the anterior gastric wall.

	Midcorpus Electrode Set 1	Electrode Set 1 Electrode Set 2	Electrode Set 2 Electrode Set 3	Electrode Set 3 Electrode Set 4
Distances (cm):	4.3	3.9	3.6	3.2

TABLE 2. Number of electrodes in a given circumferential electrode set and distances between individual electrodes in the set.

	Electrode Set 1 (Most Proximal)	Electrode Set 2	Electrode Set 3	Electrode Set 4 (Most Distal)
No. of electrodes	6	5	4	3
Interelectrode distance (cm)	3.24	3.45	3.41	2.93

The circumference of the most proximal circle of the gastric conoid on which stimulating electrodes were placed was found to be 19.48 cm. Accordingly, the six stimulating electrodes were positioned 3.24 cm apart. Table 2 shows the number of stimulating electrodes and the interelectrode distances in each of the four sets of stimulating electrodes used in the model.

Figure 1 shows a simulated pacing session produced by

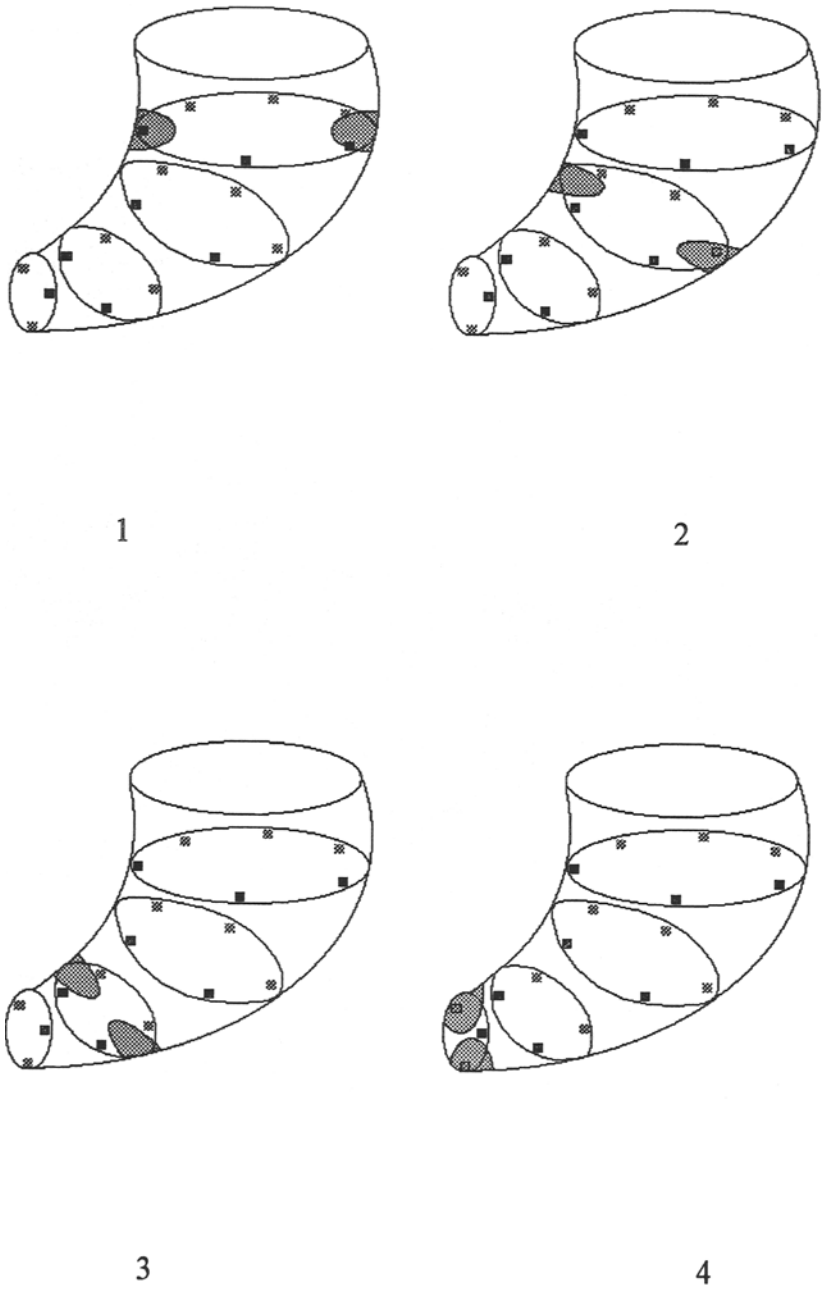

FIGURE 1. Four-step stimulation session starting with stimulating voltage applied to the proximal circumferential electrode set 1 and ending with stimulating voltage at the distal electrode Set 4. Shadowed areas indicate the places of circumferential contractions. The electrodes with lighter color are implanted on the posterior gastric wall.

the model. Phase-locking the electrical stimuli that produced simulated contractions is shown in Fig. 2.

Results from Testing the Model

When testing the concept of producing local, nonpropagated contractions on the two dogs, low-frequency voltages (DC—0.5 Hz) failed to produce visible contraction regardless of the duration of the applied stimuli. Amplitudes above 5 V (peak to peak) were found to be dangerous for the tissue. Whitening of the tissue around the electrodes was noted when stimulating amplitudes were between 5 to 8 V, and higher amplitudes produced visible burns.

Stimulating voltages of 5, 50, and 500 Hz applied for 2 to 4 sec produced quite strong circumferential nonpropagated contraction. Amplitudes up to 20 V did not produce visible damage to the tissue. The response of the smooth muscle to trains of rectangular impulses at 50 Hz (peak-to-peak amplitudes: 10 to 20 V) was found to be optimal and always produced visibly strong local circumferential contraction between and slightly beyond the two stimulating electrodes.

Blocking the cholinergic neurotransmitters with 3.0 ml of atropine, however, abolished or dramatically reduced the significance of the invoked contractions in the whole frequency range of stimulation.

DISCUSSION

In this study, we suggest a theoretical method that could be used in real-life gastric pacemaking. The method is based on the conoidal dipole model of GEA described earlier (6) and implies that artificially propagated gastric contractions can be produced using circumferential sets of stimulating electrodes and phase-locking of the applied stimuli. The suggested model derives the geometry of the stimulating electrodes, the electrode positions, and the actual phase-locking of the stimulating voltages.

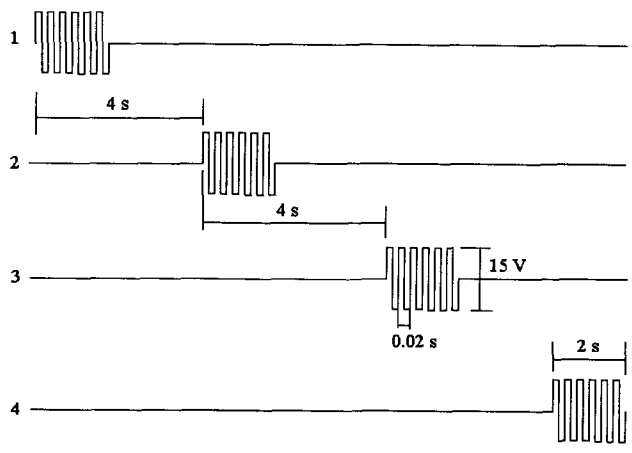

FIGURE 2. Phase-locking the stimulating voltages applied to different circumferential electrode sets starting with the most proximal Set 1. Two-second trains of 15 V (peak to peak), 50 Hz bipolar voltages were used.

Testing our approach on two dogs suggested that: (a) the hypothesis that high-frequency bipolar voltage can be used for local "*in vivo*" stimulation of gastric smooth muscle is quite realistic; (b) the response to stimulation with frequencies higher than 5 Hz is mainly cholinergic in nature and is abolished or significantly suppressed by atropine; and (c) stimulation with a train of 50-Hz rectangular impulses (peak-to-peak amplitude: 10 to 20 V) for ~2 to 4 sec can induce almost immediate strong nonpropagated contraction.

Producing artificially propagated contractions does not necessarily mean that an adequate gastric emptying would be obtained, nor does it mean that the set of stimulating electrodes used in this model should not be modified as real-life experiments on humans indicate. Moreover, the problem of synchronizing the artificially contracting stomach with (possibly) spontaneously contracting duodenum remains open. Practically, this means that biofeedback from the duodenum would probably be required to control gastric electrical stimulation. If the proximal duodenum is mechanically inactive, stimulation synchronized with the one in the stomach could be required as well.

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