Transscleral Microwave Cyclodestruction

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A 4.6-gigahertz (GHz) microwave applicator was used to ablate the ciliary body in rabbit eyes. High-frequency electromagnetic radiation provides a favorable dose distribution to induce local heating of the ciliary body. For treatment, a 3-mm diameter disc-shaped applicator was placed on the conjunctiva and over the ciliary body. Conjunctival temperatures were monitored during treatment with a built-in thermocouple thermometer located at the center of the disc-shaped antenna. This allowed direct measurement (dosimetry) of the conjunctival temperature during treatment. Using this microwave-based heat-delivery system, doses in a range of 60°C for 30 or 60 seconds appeared to cause ciliary body damage with relative sparing of the conjunctiva and sclera. Invest Ophthalmol Vis Sci 31:2151–2155, 1990

Ciliary body destruction continues to play an important role in the treatment of refractory glaucoma.1–5 Although cyclocryotherapy has been the clinical standard,2,3 therapeutic ultrasound4,5 and neodymium:yttrium aluminum garnet (Nd:YAG) cyclotherapy (both contact and noncontact) are now being investigated as alternate treatments for refractory glaucomas.6–11

We are investigating microwave radiation as an energy source in the production of thermal damage to the ciliary body.12 Advantages of microwave heat induction are: (1) the depth of heat treatment can be modulated by frequency selection,12–14 (2) tissues with relatively low water content (eg, sclera) should remain relatively unaffected by microwaves,15,16 and (3) microwave technology/components are relatively inexpensive.

Microwave applicators have been investigated for hyperthermic treatment of experimental intraocular tumors in rabbit eyes.17,18 In these experiments 8–10-mm (diameter), dish-shaped microwave applicators were placed on equatorial sclera to produce episcleral temperatures of (45 and 47°C).17,18 Microwave-induced intraocular heating was shown to cause chorioretinal damage with relative sparing of the rabbit’s sclera.17,18 Similar heat-related chorioretinal damage has been noted in clinical trials.19 It seemed reasonable to assume that if these applicators were placed on the sclera beneath the ciliary body, cyclodestruction would result.

A smaller microwave aperture was necessary for heat treatment of the pars plicata. We designed a microwave antenna to induce heat in a 3-mm diameter circular area of the eye wall. It was placed on the conjunctiva in the desired location for treatment, and temperatures were monitored during treatment with a built-in thermocouple thermometry system.

We did the first study to our knowledge on the effects of a microwave delivery system designed to heat the ciliary body. We examined the effects of a spectrum of thermal doses (temperature × time) measured at the conjunctiva (boundary temperature) at a location which should include the ciliary body in the treatment zone.

Materials and Methods

Microwave Applicator

The gun-shaped microwave applicator was a loaded-monopole-antenna design (Fig. 1). A length of semirigid coaxial cable was used with a 1-mm section of the outer conductor removed from one end. Then a 25-mm diameter metal disc with a central hole (for the cable) was affixed 30 mm from the opened end of the cable. A second disc 3 mm in diameter also with a central hole (for the cable) was affixed to the center conductor at the end of the coaxial line. The diameter of the smaller disc and the gap between the disc and the outer conductor of the cable produced a reactivity that allowed currents in the cable to flow on the outer conductor of the cable. These physical dimensions.
Flexible Coaxial Cable

Fig. 1. (A) The hand-held, contact microwave cyclothermia device. (B) A schematic design of the microwave cyclothermia device showing its component parts.

produced an efficient transfer of microwave energy to tissues at a frequency of 5.8 gigahertz (GHz). Then a cone of Teflon (Etok Plastics, Trenton, NJ) material was placed to fill the space between the two discs in an effort to protect tissues that would otherwise come in contact with the sides of the antenna. This additional material changed the frequency to 4.6 GHz (Fig. 1). This applicator was designed to heat effectively to a depth of 2–3 mm.

The temperature of the tissues in contact with the tip of the applicator were monitored with a special copper-constantan thermocouple junction (Omega, Stamford, CT). This assembly was a pliable stainless-steel sheathed thermocouple with the thermocouple wires insulated from themselves and the metal sheath. The diameter of the sheath was chosen so that the thermocouple assembly could replace the center conductor of the coaxial cable. A standard microwave 90° cable connector was modified so that the thermocouple assembly could pass straight through the connector. Thus the microwave energy was introduced through the 90° arm of the connector (Fig. 1).

Our studies required the use of 12 Giant Flemish rabbits. Twelve eyes were treated with microwave heating, and one served as a control. Experiments were performed in a manner consistent with the ARVO Resolution on the Use of Animals in Research. Before treatment, 3–5 kg rabbits were anesthetized with intramuscular xylazine hydrochloride 20 mg/kg and ketamine hydrochloride 40 mg/kg. Then topical proparacaine hydrochloride was dropped onto the treatment sites.

For treatment, we used the gun-shaped 4.6-GHz microwave applicator with a circular aperture (tip) 3 mm in diameter. The microwave cyclothermia tip was placed so that its peripheral edge approximated the posterior aspect of the corneal scleral limbus (Fig. 2). A thermocouple (thermometer) was built into the center of the cyclothermia tip so that it would touch...
the conjunctiva during treatment. Temperatures were continuously monitored, using “field-off” techniques to minimize microwave-induced artifacts. Temperatures of 55, 60, 65, or 70°C were generated for 15-, 30-, or 60-sec durations. All eyes received either three or six spots of treatment and were evaluated at 1 hr, 24 hr, or 7 days follow-up.

Rabbits eyes were enucleated under anesthesia to minimize the possibility of artifactual changes associated with our method of sacrifice or postmortem alterations. Enucleated eyes were placed in a minimum of 30 ml of cold buffered 10% formalin solution. Then the rabbits were killed with intracardiac pentobarbitol sodium. After 24 hr the eyes were vertically sectioned to transect the treatment sites. All specimens were alcohol dehydrated, fixed in paraffin, sectioned, and stained with hematoxylin and eosin for light microscopy.

Results

We found this microwave applicator to be capable of causing conjunctival, scleral, and ciliary body damage. Gross examinations with fluorescein were used to describe conjunctival effects. Increasing thermal doses (temperature $\times$ time) measured at the conjunctiva appeared to induce increasing thermal damage. Evaluation of rabbit eyes within 1 hr of treatment revealed no or minimal observable lesions at 55 and 60°C, whitening of the conjunctiva at 65°C for 60 sec (Fig. 3), to frank conjunctival necrosis at 70°C for 15 sec. No late conjunctival necrosis was noted; all lesions followed for 1 week resolved.

Histopathologic evaluations were performed on ten of 12 treated rabbit eyes (two were destroyed in processing) (Table 1). Conjunctival findings ranged from mild subconjunctival mononuclear infiltrates to frank conjunctival necrosis. Scleral findings ranged from no observable effect to thickening or scleral collagen disorganization. The amount of scleral change seemed related to thermal dose. Although one specimen had scleral collagen disorganization without sclerocyte dropout at 55°C for 15 sec followed for 1 week before enucleation, three other specimens treated at 55°C for 15, 30, or 60 sec had no apparent scleral collagen damage or loss of sclerocytes. The most common scleral finding was one of no change to possible thickening (as noted at 60°C for 60 sec and at 65°C for 30 and 60 sec). In all cases the appearance and numbers of sclerocytes in the radiated zone were comparable to adjacent untreated sclera.

Ciliary body damage was noted to increase with increasing temperatures. On examination of the nonpigmented ciliary body epithelium, we first noted intercellular edema, then moderate attenuation, and finally marked attenuation (Fig. 4). We also noted a trend of increasing edema at the base of the ciliary body, increasing separation of the nonpigmented and pigmented ciliary body epithelium, pigment liberation, and focal pigment epithelial detachments (Fig. 5). Complications included one eye with ciliary body necrosis with hyphema at 65°C for 15 sec (Fig. 6) and erythema on four rabbit eyelids.

Discussion

Microwave radiation is known to heat high water-content tissues preferentially (eg, muscle) compared with low water-content tissues (eg, fat).12-14 Therefore there should be selective heating of the high water-content ciliary body compared with the relatively low water-content sclera.15,16 The relative thermotoler-

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Time (sec)</th>
<th>Follow-up</th>
<th>Effect</th>
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<tbody>
<tr>
<td>55°C</td>
<td>15</td>
<td>1 hour</td>
<td>Conjunctival edema. Separation of the epithelial layers of the ciliary body.</td>
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<tr>
<td>55°C</td>
<td>15</td>
<td>7 days</td>
<td>Conjunctival necrosis. Slight scleral collagen disorganization.</td>
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<tr>
<td>55°C</td>
<td>30</td>
<td>7 days</td>
<td>No apparent effect.</td>
</tr>
<tr>
<td>55°C</td>
<td>60</td>
<td>7 days</td>
<td>Mild intercellular edema of the nonpigmented ciliary body epithelium. Separation of the pigmented epithelial layers. Limbal infiltrate.</td>
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<tr>
<td>60°C</td>
<td>60</td>
<td>7 days</td>
<td>Nonpigmented ciliary epithelium had focal intercellular edema and necrosis. Mild separation of the 2 ciliary epithelial layers. Focal pigment epithelial disruption. Possible scleral thickening. Mild vitreous hemorrhage.</td>
</tr>
<tr>
<td>65°C</td>
<td>15</td>
<td>1 hour</td>
<td>Specimen destroyed in processing.</td>
</tr>
<tr>
<td>65°C</td>
<td>15</td>
<td>1 day</td>
<td>Specimen destroyed in processing.</td>
</tr>
<tr>
<td>65°C</td>
<td>15</td>
<td>7 days</td>
<td>Severe necrosis of the ciliary body with secondary hyphema formation. Moderate attenuation of the nonpigmented ciliary epithelium. Separation of the epithelial layers. Marked edema of the ciliary body. Possible scleral thickening.</td>
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<tr>
<td>65°C</td>
<td>30</td>
<td>7 days</td>
<td>Moderate attenuation of the nonpigmented ciliary epithelium. Separation of the epithelial layers. Marked edema of the ciliary body. Possible scleral thickening.</td>
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<tr>
<td>65°C</td>
<td>60</td>
<td>7 days</td>
<td>Scleral thickening. Separation of ciliary epithelial layers.</td>
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<tr>
<td>70°C</td>
<td>15</td>
<td>1 day</td>
<td>Conjunctival necrosis. Prominent separation of the ciliary epithelial layers.</td>
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**Fig. 4.** (left) The specimen heated to 55°C for 15 seconds and enucleated 1 hour after treatment demonstrated early edema between the pigmented and nonpigmented ciliary epithelium. Note the ciliary epithelium was of normal height. Hematoxylin and eosin (×80). (center) The specimen heated to 60°C for 60 seconds and enucleated 7 days after treatment displayed separation between the pigmented and nonpigmented ciliary epithelium (arrow), with mild liberation of pigment from the pigmented ciliary epithelium. There was mild to moderate edema of the subjacent connective tissue of the ciliary processes. Hematoxylin and eosin (×80). (right) The specimen heated to 65°C for 30 seconds and enucleated at 7 days after treatment displayed extensive pigment liberation of the posterior ciliary epithelium, marked thinning of the nonpigmented ciliary epithelium (arrows), and continued increased separation between the epithelial layers was present. Marked edema of the connective tissue of the ciliary processes was noted. Hematoxylin and eosin (×110).

**Fig. 5.** In the specimen heated to 65°C for 60 seconds and enucleated 7 days after treatment, scleral thickening the focal detachments of the ciliary epithelium were noted (arrows). Hematoxylin and eosin (×40).

**Fig. 6.** In the specimen heated to 65°C for 15 seconds and enucleated 7 days after treatment, the authors noted severe necrosis of the ciliary body with prominent pigment dispersion and secondary hyphema formation. Hematoxylin and eosin (×110).
ance of sclera and cornea has been demonstrated with conductive and microwave heat delivery systems.\textsuperscript{17-22} Hyperplasia (scleral thickening) as a response to low level heating of rabbit sclera has been demonstrated in experiments with conductive heaters.\textsuperscript{20-22}

In this experiment we noted possible scleral thickening in four treated eyes, although in all cases the density and morphology of sclerocytes in the treatment zone was comparable to untreated rabbit sclera. Although scleral collagen disorganization was noted in one specimen, the sclera tolerated thermal doses which produced edema, attenuation, and necrosis of the ciliary epithelial layers.

Advantages of this microwave cyclothermia applicator were that: (1) it allowed for dosimetry (direct temperature measurement at the conjunctival surface during treatment), (2) there was no need for a coupling medium between the energy source and the eye, and (3) direct application eliminated the need for an aiming mechanism.

We showed that this applicator can produce ciliary body damage in normal rabbit eyes. It appeared that the thermal tolerance of the conjunctiva did not exceed 65°C and that heat doses in a range of 60°C for 30 or 60 sec caused ciliary body damage with relative sparing of the conjunctiva and sclera. We conclude that with a microwave heat-delivery system, it may be possible to damage the ciliary body with relative sparing of the conjunctiva and sclera.

Key words: heat, microwave, conjunctiva, sclera, ciliary body

References