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The Gamma Knife in ophthalmology. Part two – other ocular diseases

Zastosowanie Gamma Knife w okulistyce. Część druga – inne schorzenia okulistyczne

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Summary: The Gamma Knife was designed by Lars Leksell in the early 1950's. It gave rise to a new discipline of medicine – stereotactic radiosurgery. Main use of Gamma Knife in ophthalmology – discussed in the first part of this paper – is non-invasive treatment of uveal melanoma. Another uses of LGK in ophthalmology cover choroidal hemangioma, orbital tumors and even choroidal neovascularization.

Key words: Gamma Knife, stereotactic radiosurgery, choroidal hemangioma, age-related macular degeneration (AMD).

Streszczenie: Gamma Knife zaprojektowany w latach 50. minionego stulecia przez Larsa Leksella dał początek nowej dziedzinie zwanej radiochirurgią stereotaktyczną. Główne zastosowanie Gamma Knife w okulistyce polega na bezinwazyjnej terapii czerniaków naczyniówki, zostało to omówione w pierwszej części artykułu. Pozostałe zastosowania obejmują radiochirurgię malformacji naczyniowych, guzów oczodołu, a nawet wysiękowej postaci zwyrodnienia plamki związanego z wiekiem. Leksell Gamma Knife znajduje zastosowanie także w radiochirurgii malformacji naczyniowych, guzów oczodołu, a nawet wysiękowej postaci zwyrodnienia plamki związanego z wiekiem.

Słowa kluczowe: Gamma Knife, stereoradiochirurgia, naczyniak naczyniówki, zwyrodnienie plamki związane z wiekiem (AMD).

Vascular malformations

Choroidal hemangioma (CH) is a benign hamartomatous tumor which may be circumscribed or diffuse. CH does not become malignant and turns symptomatic when complications develop e.g. exudative retinal detachment (1). Therapeutic options for choroidal hemangioma are: observation, transpupillary thermotherapy (TTT), photodynamic therapy (PDT), photocoagulation, cryotherapy, anti-VEGF injections, radiosurgery (2, 3). Treatment is applied only in cases with retinal detachment (RD) and vision deterioration, and the goal of treatment is subretinal fluid absorption (4, 5).

The Gamma Knife mechanism of action consists of endothelial cell destruction and micro-obliterations of capillaries, hence the idea of GKRS treatment for choroidal malformations. Kim et al. (4) presented seven patients (three with circumscribed and four with diffuse hemangioma) treated with a Gamma Knife. In all cases exudative retinal detachment resolved completely within 1.5 to 6 months, even if radiation „covered" only a part of the diffuse hemangioma. Due to macular reattachment vision improvement was observed ($p = 0.018$). The single marginal dose was 10 Gy in all patients. It was estimated that during treatment the macula absorbed radiation of 3.7–14.7 Gy, while the optic nerve 4–9 Gy. No post radiation symptomatic complications were reported during follow-up (on average 44 months). The single dose 10 Gy was also applied by Kong et al. (6) for CH treatment in three young patients. Tumor size and subretinal fluid volume decreased during the entire follow-up period (of 18–36 months), visual acuity slightly improved and no post radiation side effects were noted. Song et al. (5) treated with GKRS three hemangiomas with concomitant RD covering more than two retinal quadrants, obtaining reattachment of the retina in two cases (in two and five months respectively). The third patient with total retinal detachment needed pars plana vitrectomy. GKRS was a secondary treatment in this series (after TTT) and led to a reduction of the tumor thickness by 40%. However, a much higher dose was applied on the tumor margin than in previous reports (26.7 Gy), no complications related to eye irradiation were recorded. Unfortunately in two patients there was a slight decrease in vision during the one-year follow-up. The authors emphasize that the Gamma Knife proved to be more effective in comparison with other radiosurgery techniques, due to convenience, possibility of large tumors precise irradiation, and minimal radiation dose dispersion on adjacent tissues. The use of a Lexel Gamma Knife allows treatment of choroidal hemangiomas of sizes unmanageable with laser therapy or brachytherapy (7). GKRS can be an effective and safe alternative for CH treatment, nevertheless further randomized studies with larger groups are necessary.

Age-related macular degeneration

Wet form of AMD with subfoveal choroidal neovascularization (CNV) is responsible for most cases of severe vision loss in this disease. Methods of CNV treatment are limited. In 2006 FDA and then, in 2007, EMEA approved ranibizumab (Lucentis, Novartis) for the treatment of wet macular degeneration. Despite promising results, intravitreal injections are invasive, frequent and expensive therapy.

At the end of the 90's, Finger et al. (8) published moderately optimistic reports about treatment of CNV using external beam radiation therapy. Other authors followed in his steps, based on the theory of destroying pathological vessels by the beams of protons or photons (9).

Haas et al. (10) presented a group of 10 patients with classic subfoveal CNV treated with Gamma Knife. None of them experienced radiation-related side effects during the one-year follow up. A single margin dose of 10 Gy stabilized visual acuity in six patients, but four experienced a decrease of BCVA of three or more lines. Hayashi et al. (11) reported therapy of three neovascular membranes with LGK (model C). Two of them were demonstrated with traditional contrast-enhanced MRI (10 Gy in 80% isodose), but one was estimated with an extremely precise time-of-flight MRI (TOF MRI) imaging sequence (15 Gy in 60% isodose). In all three cases no complications occurred and CNV was stable. Despite the benefits, GKRS is not a popular treatment option in exudative AMD, probably because of difficulties in precise imaging of the lesion using traditional MRI.

Orbital tumors

Gamma Knife steroradiosurgery is related to two disciplines: ophthalmology and neurosurgery. Both disciplines meet in treatment of orbital tumors. Orbit includes many structures (e.g. bone walls, eyeball, vessels, lacrimal gland or fat) and orbital tumors may arise from any of them. Visual deterioration and diplopia can be caused by compression of the eyeball, optic nerve, nutrient vessels or extraocular muscles. Choice of the treatment (microsurgery, radiotherapy, radiosurgery) depends on tumor size, location and grade of malignancy (1), but in many cases complete surgical tumor removal is not possible. Xu et al. (12) observed a group of 202 patients with benign and malignant orbital tumors (mean target volume of 5.4 cm^3). LGK was used in a single or two sessions (fifteen patients), 5-year tumor control rate was achieved in 93.5% of cases. Four patients needed additional surgical treatment due to progression. The administered marginal dose ranging from 10 to 40 Gy depended on the type and extension of the lesion. Symptoms resolved in 89.6% of patients, but complications related to GKRS were also noticed. Optic pathways absorbed doses oscillated between 6 and 16 Gy, and 23 patients experienced visual impairment. Transient side effects included blepharoconjunctivitis and eyelid edema. Stafford et al., that the risk of optic neuropathy after SRS is higher, when the optic tract receives doses greater than 12 Gy. Kim et al. (13) observed a smaller group of 15 patients, treated with gamma knife radiosurgery. The mean follow-up time was 20.9 months. Seven of them underwent fractionated GKRS (the mean cumulative marginal dose was 20 Gy), and eight of them received a median dose of 14 Gy in one session. Tumor control was achieved in 80% of patients, and the results were comparable between the above-mentioned groups. Three patients underwent additional surgical treatment due to tumor progression; in two of them visual acuity decreased. One case of optic neuropathy was observed in this study. Tumor-associated symptoms like headaches or ocular pain resolved in all patients.

Modern techniques of streoradiosurgery result in better control of the eye diseases. Before the GKRS era many ocular and orbit tumors were beyond our reach due to their risky location. Currently an extensive literature regarding GKRS confirms that Gamma Knife is a reliable, precise and safe tool, both for patients and medical staff. Careful patient selection and confident doctor–patient relationship play an important role in effective treatment. The key issue for accurate dose planning is very high resolution imaging. Doses of radiation have to comply with tumor size, its location and the risk of ocular side effects. Promising results of Gamma Knife use in ophthalmology, presented in this review, give us hope for effective treatment of many ocular diseases in future.

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 ISSN 0023-2157 Index 362646

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The study was originally received 25.07.2013 (1453 cz. 2)/
Praca wpłynęła do Redakcji 25.07.2013 r. (1453 cz. 2)
Accepted for publication 14.04.2014/
Zakwalifikowano do druku 14.04.2014 r.

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