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Light seeing in patients with brain tumors and head and neck malignancies treated with radiotherapy

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Summary. *Background:* Reaching a better understanding of light vision in radiotherapy patients. *Materials and methods:* 20 patients with brain tumors and head and neck malignancies who received radiotherapy and experienced any kind of light or color vision during radiation treatment. All the components of visual pathway were contoured. *Results:* 11 patients were male and 9 were female (median age: 56 years). The range of dose/fraction and total prescribed dose were 1.8-3Gy and 36-70.4Gy respectively. Twelve patients reported white, 11, blue, 2, yellow and 2, gray color visions. Seven patients experienced more than one color, while 2 patients did not attribute any special color to their experiences. Four patients had a kind of smell experience and 1 patient had a taste experience. *Conclusion:* Cherenkov radiation in eye balls may be the origin of light seeing experiences in patients receiving radiation treatment for head and neck malignancies, since treatmentsareperformed with ionizing radiations with energycapable to produce this effect. Also this effectmay be due to phosphenes produced by radiation treatment in different parts of the visual pathway (from retina to visual cortex). In order to investigate the mechanism of this phenomenon in patients and to define a radiation dose threshold – if the origin of this phenomenon is phosphenes produced in visual pathway – larger studies are needed.

Key words: phosphene, Cherenkov radiation, radiotherapy, visual pathway

Introduction

Our visual system not only mediates information about the visual environment but it is also capable of generating pictures/lights of nonexistent visual worlds within the brain as illusions, dream pictures and visual hallucination (1). The brain can also internally generate ultra-weak light signals. These signals can become conscious if they exceed a distinct threshold in the visual system (1).

A phosphene is a phenomenon characterized by the experience of seeing light without light actually entering the eye, especially when dark adapted (2, 3). The word *phosphene* comes from the Greek words *phos* (light) and *phainein* (to show) (2). Phosphenes can be directly induced by mechanical, electrical or magnetic stimulation, various drugs, stress, high-energy ionizing radiation and high-energy particles, optic nerve diseases, etc in the visual pathway from retina to visual cortex (1, 4). For example, Grüsser et al. showed that pressure on the eye results in activation of retinal ganglion cells in a similar way to activation by light (5). Phosphenes can be points, spots, bars or chaotic structures of colorless or colored light (1, 6, 7).

Astronauts exposed to radiation in space report seeing phosphenes (8). Seeing lights has been also reported by patients treated with radiotherapy for brain or head and neck tumors. This experience may be due to the production of signals and consequently phosphenes in any part of the visual pathway as mentioned above. Radiotherapy patients, similar to astronauts report mostly blue, white and sometimes yellow light flashes (9, 10). Radiation beams can also directly excite other sensory receptors in the brain, so some patients may report other sensations, like smell or taste (11). Some researchers suggested retina as the origin of phosphenes. They believe that ionising radiations can affect biochemically on retina and this way cause light perception. Regarding the radiation dose thresholds and necessary dose rates, a wide range of $5*10^{-6}$ - $5*10^{-3}$ Gy and $1*10^{-5}$ – $1.6*10^{-4}$ Gy/sec has been mentioned in these studies respectively (3, 12). However, in these studies, retina was irradiated directly to evaluate this phenomenon. They have not been done on radiotherapy patients and there is also lack of studies evaluating the other parts of visual pathway as the probable origins of phosphenes.

But there is another justification for this phenomenon. Some investigations in space and on the ground showed that this phenomenon arise from effects of ionizing radiations inside the eye ball via Cherenkov radiation (11). These lights are then detected by retina. Cherenkov radiation is an electromagnetic radiation, usually bluish light, emitted when ionizing radiations (photons or charged particles) passes through a dielectric transparent medium at a speed greater than the phase velocity of light in that medium. The ionizing radiations polarize the molecules of that medium, which then turn back rapidly to their ground state. Due to this oscillation, electromagnetic waves (visible as blue light) are emitted. The characteristic blue glow of nuclear reactors is caused by Cherenkov radiation (13, 14). Cherenkov emission intensity increases significantly when megavoltage energies are used (15). However, for any dielectric transparent media, an energy threshold for any of the ionizing radiations has been calculated. For example, in the eye ball, photons of about 0.4 MeV or electrons of 0.26 MeV or higher energies are able to produce Cherenkov radiation that can be detected by the retina (9, 15, 16). In this study, we tried to reach a better understanding of this phenomenon through evaluating the radiation doses delivered to different parts of the visual pathway in patients receiving head and neck radiation treatment.

Materials and methods

Between April 2013 and May 2014 we asked patients with brain tumors and head and neck malignancies who received radiotherapy about experiencing any kind of light or color vision during radiation treatment. Those who reported such experiences, were asked to give a description of what they exactly saw during treatment with the help of a questionnaire (Suppl. 1). These patients had experienced such phenomena neither before the beginning radiation treatment nor in the intervals of radiation sessions. All of the patients were in good condition (Karnofsky Performance Status >60). In order to contour the visual pathway components precisely, the best imaging is MRI rather than CT scan. Thus, we selected only patients who had brain MRIs as well as planning CT scans. Finally 20 patients fulfilled the inclusion criteria. Eclipse version 10 planning system (Varian Medical Systems, Palo Alto, CA, USA) was used for this study. In the planning system, all the components of visual pathway including lenses, eye balls, retinas, optic nerves, chiasm, optic tracts, optic radiations and visual occipital cortexes were contoured under the supervision of a neuro-radiologist. Figure 1 shows these contoured components in the planning system in one of the patients. The radiation doses delivered to each part of the visual pathway were extracted from the planning system. We also checked if any of these components were in direct beam of radiation or not.

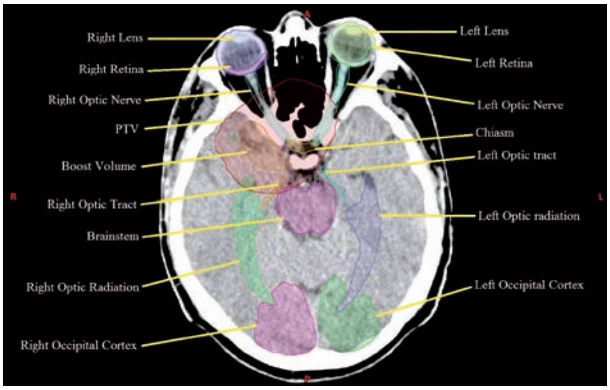

Figure 1. Components of the visual pathway (lenses, eye balls, retinas, optic nerves, chiasm, optic tracts, optic radiations and visual occipital cortexes) contoured in one of the patients. Target volumes (PTV and Boost volume) are also shown in this patients.

Results

Out of 20 patients, 11 were male (55%) and 9 were female (45%). The age ranged from 28 to77 (mean 51.4, median 56). Diagnoses and tumors' locations are shown in table 1. It is important to mention that in 8 patients between 1 to 4 components of the visual pathway were involved by the tumor before beginning the radiation treatment (Table 1). Due to a non-malignant reason, one patient had enucleating of the right eye a few years before radiation treatment. Thus in this patient right lens, right retina and right eye ball could not be contoured. Regarding the radiation treatment techniques, 7 patients were treated by VMAT (Volumetric Modulated Arc Therapy), 6 patients by IMRT (Intensity Modulated Radiation Treatment), 6 patients by three-dimensional conformal radiation treatment and 1 patient by Tomotherapy. The light vision experiences of the patients are summarized and shown in table 2. Seven patients experienced more than one color, while

Table 1. Characteristics of the tumors

	No. of patients
Diagnosis	
Glioblastoma	7
Oligoastrocytoma, grade 3	3
CNS lymphoma	2
Left sphenoid wing meningioma, grade 2	1
Tentorial meningioma, grade 1	1
Astrocytoma, grade 3	1
Astrocytoma, grade 2	1
Nasal cavity carcinoma	1
Hemangiopericytoma	1
Tonsil carcinoma	1
Parotid mucoepidermoid carcinoma	1
Tumor location	
Right frontal lobe	3
Left parieto-occipital lobes	3
Left frontal lobe	2
Left sphenoid wing	2
Right temporal lobe	2
Right cavernous sinus	1
Right tonsil	1
Left fronto-parieto-temporal lobes	1
Left parotid gland	1
Left nasal cavity	1
Tentorium (sagittal sinus)	1
Left fronto-parietal lobes	1
Left temporo-parietal lobes	1
Involvement of optic pathway components by tumor in 8 patients	
Right optic nerve, chiasm, right optic tract	
Right and left visual occipital cortex	
Chiasm, right optic tract, right optic radiation	
Right optic tract	
Left optic tract, left optic radiation, left visual occipital cortex	
Left optic radiation	
Left optic nerve, left optic radiation	
Left optic radiation	

Table 2. Summary of patients' color vision description

Patients	Description of color vision experience during radiation treatment
1	Seeing long-lasting light blue color mixed with white and short seeing of blue color at the borders of visual field in left eye. Not in every fraction
2	Blue stripe. 2 times. In every fraction
3	Blue color coming from right side of visual field. In every fraction
4	One white stripe. Not in every fraction
5	Seeing blinks similar to ECG in both eyes. In 80% of fractions
6	Blue and white flashes. In every fraction
7	Gray and white colors similar to kaleidoscope not in every fraction; seeing blue color coming from left side. In every fraction
8	White and blue colors. In the first third of every fraction
9	Seeing blue color with closed eyes as coming and going. In every fraction
10	Seeing light white color in left eye nearly. In every fraction
11	Seeing white to yellow flashes. At the end of every fraction. Afterwards feeling burning smell
12	Blue flashes in 10% of the fraction often with O_3 smell. Occurred irregularly for a few fractions, then every fraction
13	Light white color. In every fraction
14	Blue and gray waves coming from left side with gas smell. Not in every fraction.
15	Light flashes coming like a moving car in second part of the fraction. Not in every fraction
16	Blue flashes in upper part of visual field with closed eyes. In every fraction. Not seen with open eyes
17	White continuous flickers moving from left to right then from right to left. In every fraction. These flickers were glaring at two points. Temporarily blindness for a few minutes after treatment.
18	White and short flashes. In every fraction
19	Light white and wave shaped flashes. Not in every fraction
20	Flashes mostly blue (rarely changed from white to yellow and from yellow to blue). In every fraction. Additionally a strong feeling of smell and taste.

2 patients did not attribute any special color to their light seeing experiences. In total, 12 patients reported white, 11 blue, 2 yellow and 2 gray color visions. Four patients noticed kind of a smell and 1 patient a taste. 12 patients had these experiences in every fraction of treatment, 2 of them nearly in every fraction and the others irregularly. The patient whose treatment plan is shown in figure 1 had blue and white flashes in every fraction.

Regarding the treatment, all the 20 patients were treated by photon with the nominal energy of 6 MV. The nominal dose rates in our institution are up to 6 Gy/min in linear accelerators and up to nearly 9 Gy/min at Tomotherapy. The range of the total prescribed dose for the patients was 36-70.4 Gy with the mean of 56.3 Gy and the median of 60 Gy. The number of total fractions ranged between 12 and 33 and the range of dose/fraction was 1.8-3 Gy. Table 3 shows the delivered doses to any of the visual pathway components in each fraction and if any of the visual pathway components was located in direct beam.

Table 3 shows that the delivered doses to the components of the visual pathway (optic tracts, optic radiations, chiasm, optic nerves, visual occipital cortexes and retinas) are higher than the delivered doses to the ocular components (eye balls and lenses). Furthermore, the left side components seem to have received higher doses in comparison to their right side counterparts. This can be explained by the fact that in 12 patients, tumors were located at left side of the head and neck, 1 tumor in midline and 7 tumors at the right side.

Discussion

Very few studies have been done on the topic of light vision in patients receiving radiation treatment. Some researchers believe that these experiences in patients are mostly due to Cherenkov radiation, since the radiation treatment is done by the photons or electrons with energies capable to cause this phenomenon in the eye balls (9-11). Thus, if the eyes are inside the direct beam of radiation, seeing lights during the radiation treatment can be explained by this phenomenon.

Table 3. Delivered doses per fraction to the visual pathway components

	Dose range (Gy) (20 patients)			Average of dose (Gy) (20 patients)			Median of dose (Gy) (20 patients)			Locating inside target volumes (# of patients)		Locating in direct beam (# of patients)
	Dmin	Dmax	Dmean	Dmin	Dmax	Dmean	Dmin	Dmax	Dmean	PTV	GTV	
Left optic tract	0.03-1.80	0.03-2.02	0.03-1.90	0.83	1.29	1.06	0.72	1.56	1.21	8	2	19
Left optic radiation	0.02-1.91	0.03-3.02	0.03-2.20	0.62	1.44	1.02	0.42	1.52	1.05	4	5	19
Right optic tract	0.04-1.81	0.06-1.94	0.05-1.83	0.68	1.10	0.92	0.59	1.16	0.90	4	3	18
Chiasm	0.03-1.80	0.05-1.82	0.04-1.81	0.75	1.11	0.92	0.49	1.33	0.81	6	2	19
Right optic radiation	0.03-1.48	0.08-2.04	0.05-1.90	0.49	1.16	0.80	0.32	1.15	0.58	4	2	19
Left optic nerve	0.02-1.61	0.02-1.83	0.02-1.80	0.54	0.97	0.78	0.27	1.02	0.63	4	3	18
Left visual occipital cortex	0.01-1.55	0.09-3.11	0.03-2.34	0.42	1.18	0.76	0.13	1.06	0.57	5	2	20
Right visual occipital cortex	0.02-1.46	0.21-2.04	0.06-1.65	0.40	1.66	0.68	0.15	1.13	0.50	5	1	20
Right optic nerve	0.02-1.58	0.04-1.84	0.03-1.81	0.46	0.88	0.67	0.29	0.73	0.47	2	1	16
Left retina	0.01-1.31	0.02-1.64	0.01-1.44	0.23	0.72	0.49	0.15	0.60	0.25	2	1	18
Right retina	0.01-1.21	0.03-1.68	0.02-1.45	0.19	0.57	0.40	0.14	0.58	0.29	1	1	16
Left eye ball	0-1.11	0.02-1.88	0.01-1.40	0.17	0.80	0.38	0.12	0.75	0.27	2	1	19
Right eye ball	0-0.91	0.03-1.63	0.02-1.40	0.13	0.60	0.30	0.09	0.59	0.24	1	1	17
Left lens	0.01-1.33	0.01-1.42	0.01-1.38	0.19	0.26	0.22	0.13	0.17	0.15	1	0	11
Right lens	0.01-1.36	0.02-1.42	0.02-1.40	0.17	0.20	0.18	0.12	0.15	0.13	1	0	7

On the other hand, phosphenes produced by radiation treatment in different parts of the visual pathway (from retina to visual cortex), may be the origin of these experiences (see introduction). Our study shows that the doses delivered to the components of visual pathway are higher than the doses delivered to the eye balls. This difference is not surprising when we remember that a large part of these structures is located inside the target volumes of radiation treatment (Gross Tumor Volume (GTV) and Planning Target Volume (PTV)) or at least, closer to target volumes in comparison to ocular components.

Considering previous studies that focused on retina (3, 12), the delivered doses to retina in our study are much higher than what has been mentioned in these studies (not less than 0.01 Gy) (see introduction and table 3). This difference can be justified not only by the vicinity of the eye ball and radiation beams, but also by this point that in our study we evaluated radiotherapy patients who received a dose/fraction of 1.8-3 Gy around the tumor region. The same is true regarding dose rates.

In our study there is one patient whose eye balls are not inside direct beam of radiation. So it can be supposed that phosphene theory is of more importance at least in this patient, but one can argue that even in this patient the scattered radiation to the eye ball(s) may have caused the light seeing experience. Electrophysiological monitoring of the patients can be also helpful in future studies to evaluate the origin of this phenomenon (17). Anyway, in order to scrutinize the mechanism of this phenomenon in patients receiving radiation treatment in head and neck and to define a radiation dose threshold – if the origin of this phenomenon is phosphenes produced in visual pathway – larger studies are needed. Comparing dose data of patients who experience light seeing with dose data of similar patients who do not have such experiences may be another way of further evaluation of this phenomenon.

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Supplement 1. Questionnaire [translated into English]

Patient's label

Dear Patient

We want to request you to answer the following questions, regarding a scientific study:

1 – Do you have any light phenomenon during the radiation treatment?

0 Yes 0 No

2 – If so, please describe your experience:

____

____

3 – How often does this phenomenon occur?

0 in every fraction

0 irregularly

Thanks a lot for your cooperation