Each morning, the day began with a **contouring workshop**. Ependymoma, medulloblastoma, and Ewing sarcoma were presented. For many of the individual sessions, described below, there were interactive components wherein the audience had individual "clickers" and could express their opinions on the questions posed. The audience could then see the results of the "votes" on a large screen.

The 2015 meeting opened with **welcoming remarks** by the President of PROS, Dr. R. D. Kortmann, and the chair of the local arrangements planning committee, Dr. L. Zadravec Zaletel.

In the opening symposium, there were presentations on the normal anatomy and physiology of **bone growth and development**, a review of the clinical data on interruption of bone growth in children by radiation therapy, a review of growth deviations such as kyphosis and scoliosis caused by radiation therapy to bone and soft tissue, and the impact of radiation techniques upon growing bone including the differential effect on different epiphyseal growth plates.

The next sequence of presentations were **brief summaries of submitted papers**. They included a demonstration that the patterns of failure in rhabdomyosarcoma, treated with proton therapy, showed that failures at the margins of the field were uncommon. This implies that there is not a contribution to tumor failure by proton field margin under-dosage. There was a substantial discussion as to whether an elevated RBE at the distal edges of proton beams might be the present or potential cause of normal tissue injury. Two speakers confirmed that re-irradiation of childhood brain tumors can be a useful palliative therapy; either with photons or protons.

The next symposium addressed **current practices in proton therapy**. In rhabdomyosarcoma, there are many situations in which photon therapy gives a perfectly acceptable dose distribution and there are some situations in which protons appear to give a superior dose distribution. The attendees learned about a single room proton facility in St. Louis, Missouri, USA constructed for US $30 million. In the US there are 14 proton units and another 10 under construction. In Europe there are 8 proton units and another 17 either under construction or in various phases of planning. Assuming a population of 640 million in Europe in the areas served by proton units v 320 million in the US, this calculates as 1 machine per 13 million in the US by 2010 v. 1 machine per 25 million in Europe by 2019.

The next symposium centered upon the **importance of quality assurance in clinical trials** involving radiation therapy. It was repeatedly shown that poorer outcomes were related to protocol violations and that a robust quality assurance process, including pre-treatment review, reduces the number and severity of quality violations and leads to improved patient outcomes. Most tumors are radio-resistant if you miss them.

The last symposium of the afternoon described the relative paucity of radiation therapy facilities in **low and middle income countries**; the high pediatric cancer morbidity and mortality rates in these countries related to a relatively young population, delay in diagnosis, and poorer treatment facilities; and efforts to ameliorate the situation through educational exchange programs and on-line education.

After the presentation of **honorary PROS memberships** to Drs. G. D'Angio and B. Jereb, the group retired to a walking tour of the lovely and historic center of Ljubljana.
Reconvening the next day, June 26, the program began with an update on SIOP brain tumor trials.

**Low Grade Gliomas (LGG)**

The speaker began with a review of low grade glioma studies. The German HIT LGG 96 trial stratified patients who were to be given non-surgical treatment. Brachytherapy was given if possible. If not and the patient was < 5 years of age they received chemotherapy. If >5 years of age there were externally irradiated. At time of tumor progression there was a cross-over. The 5 y EFS was 67% for RT first and 57% for chemotherapy first and the 5 y OS was, respectively, 92% and 85%. This study was followed by HIT LGG 2004. If the child had no symptoms/no progression then the strategy was to watch. If it was indicated to treat and no surgery was to be done and the child was <8 years of age then chemotherapy was given. If the child was > 8 years of age then 54 Gy was given. A small number of patients were treated with brachytherapy. PFS at 7 y is 76% for RT first and 45% for chemotherapy first, 7 year OS was 88% and 89%, respectively.

Pilocytic astrocytomas have a lower rate of malignant transformation than other low grade gliomas. For pilocytic astrocytoma <54 Gy is better than a higher dose. The same results were seen for grade 2 astrocytomas whether measured by PFS or OS.

For brachytherapy the 7 year PFS was 82% v. 67% PFS for external beam radiation therapy. HIT LGG 20xx is studying different kinds of radiotherapy techniques and a dose reduction from 54 to 50.4 Gy (Dr. Saran in the UK gives 50 Gy at 1.67 Gy for low grade gliomas which is what Julian Bloom did)

It is worth studying the quality of survival in low grade glioma patients.

Some US institutions use 10 years as an age cut-off for radiotherapy for low grade gliomas.

**Ependymoma**

Surgery has the greatest role to play in terms of outcome. An inoperable patient at institution A is not the same as an inoperable patient at institution B.

5 year survival in infants is 40-60% focusing on a chemotherapy only approach.

Usually the dose is 54 - 66 Gy but some give 70 Gy at 1 Gy bid.

Current European studies following the general guidelines are if the patient is post-operative, > 12 months of age, and no measurable disease then evaluate the efficacy of post RT chemotherapy. If > 12 months of age and measurable disease give phase II chemotherapy and evaluate the efficacy of a radiotherapy boost. If the patient is < 12 months of age and not eligible to get RT then a randomized phase II trial of myelosuppressive v. nonmyelosuppressive chemotherapy is being considered. If the patient is not included in one of the interventional studies then they are observed. The plans for external beam radiotherapy are CTV = GTV + 0.5 cm and add 0.3-0.5 cm for PTV and then an 8 Gy in 2 fraction boost after the initial radiotherapy with CTV=GTV and then add 0.2-0.3 cm for PTV.

The COG is asking a randomized question about chemotherapy after RT.

**PNET/Medulloblastoma**

Medulloblastomas are biologically different from supratentorial PNET

The PNET IV trial compared 36 Gy craniospinal irradiation with cone down boosts to 60-68 Gy at 1 Gy bid + chemotherapy v. 23.4 Gy of craniospinal irradiation with a boost to 54 Gy + chemotherapy. There was no benefit to hyperfractionated radiotherapy.
In medulloblastoma biology is important. Patients with activated Wnt pathway do well but Wnt is more predictive in <18 years of age than >18 years of age. Maybe Wnt+ patients will do equally well with a lower dose?

For low risk patients who are B-catenin + and Wnt+ they will get 18 Gy of craniospinal irradiation and what I believe the speaker described as a 30.6 Gy boost and low dose chemotherapy compared to 23.4 Gy of craniospinal irradiation followed by a 30.6 Gy boost + chemotherapy.

They are still debating a high risk protocol. They are thinking along the lines of 36 Gy of conventional craniospinal irradiation v. HART 39 Gy and then a boost.

**Germinoma**

EFS better with CSI v. chemotherapy and focal irradiation but there may not a difference in OS. They give chemotherapy and assess the response: CR gets 24 Gy WVI, PR gets 24 Gy WVI + 16 Gy boost, SD gets re-operation and if a total resection 24 Gy WVI and a boost of 16 Gy and if not a total resection then 24 Gy WVI followed by a 30 Gy boost.

AFP that is >1000 is a bad prognostic sign.

The next session contained brief presentations of submitted papers. They included the demonstration of considerable cranio-caudal motion of the kidneys as the result of respiration which can affect IMRT. There were very fine presentations of the use of frameless surface image guided stereotactic radiosurgery in children and another on the effect of IMRT plus chemotherapy for the treatment of carcinoma of the nasopharynx in children and how that treatment affects thyroid volume and thyroid hormone production. There were also presentations on the effect of thoracic radiotherapy on normal lung function and the risk of scoliosis after craniospinal irradiation.

The lunchtime symposium carefully described the technique of image guided radiation therapy in children. There were highly interesting presentations which described the potential for a child receiving a 2-3% increased total radiation dose because of frequent portal imaging associated with IGRT and how Kv IGRT CT could give 450-840 cGy to bone over six weeks of radiotherapy. IGRT allows about a 3-5 mm margin around the tumor but you have to think about whether you are going to image every day or every other day during the course of radiotherapy.

A smaller margin spares more normal tissue and has a lower risk of second malignant neoplasms at the price of higher radiation exposure from repetitive on-line portal imaging for IGRT which can create a higher risk of second malignant neoplasms.

The next symposium included presentations from France, Germany, and the US on the establishment, data collection techniques, and outcomes of large-scale late effects of therapy registries. This was following by a summary of the European "PanCare" late effects registry.

The next session addressed challenges to the education of residents in pediatric radiation oncology and US, Canadian, Australia/New Zealand, UK, and other European curricula for residency training.

The day closed with the gala banquet at the Ljubljana Castle.
We resumed on Saturday morning with presentation of complex cases from around-the-world and audience participation with "clickers".

This was followed by a very fine presentation on the treatment of carcinoma of the nasopharynx in children from the Cairo Children’s Hospital and two interesting papers on the use of volumetric modulated arc therapy for medulloblastoma.

PROS will convene again for its international meeting, in two years, in Izmir, Turkey.

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