Results: Results: in the 4 groups the results in terms of D90 are respectively 123±32Gy, 146±28Gy, 153±23Gy, 166±17Gy, as shown in Figure 1. The dose fall-off in terms of D90 is respectively 58Gy, 43Gy, 37Gy, 21Gy (as shown in Figure 2) and in terms of V100 17%, 10%, 8%, 4%. In the last group the mean theoretical D90 and V100 are 187Gy and 99%, against a real implant evaluation of 186Gy and 99% and the maximum urethra dose is 210Gy in the planning and 219Gy at the end of the implant. In the 30% of the patients of the “real-time” group we changed the number of seeds or needles composition during the implant, to reach the desired constraints and PTV coverage.

Conclusion: Conclusion: our work shows the impact of the “image-guided” technology evolution on the dose fall-off both in terms of D90 and V100. Moreover, we show how the “real-time” method allows to change the “theoretical” plan during the implant, to reach the recommended constraints and PTV coverage [1].

PO-0979
LBTB control and toxicity for Favorable and Intmed Risk pts using real time IO-PSI prostate BT alone
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Purpose or Objective: We initially reported biochemical control rate of 97% at 4 years of followup (Brachytherapy, 2009), which highlighted our methodology of limiting needle trauma, relying on Intra-operative, Real-Time computer assisted IO (Inverse Optimization) to reduce the number of sources and total activity without compromising dosimetric quality. This update was performed to confirm our earlier favorable BFSS outcomes.

Material and Methods: Between 2001 and 2013, 491 patients underwent real-time IO-PSI. Only patients with a minimum of 2 years of follow-up treated without supplemental IMRT were the subject of this analysis (N=315). Our dose objectives and constraints for real-time IO-PSI have previously been published and remain unchanged. The main dose objective intra-operatively was to achieve a V100 > 95% (Volume receiving > 95% of the prescribed dose). Patients were implanted with either 125I (PD=145 Gy) or 103Pd (PD =120 Gy). Toxicity was prospectively scored using the Radiation Oncology Group Toxicity scale and the International Prostate Symptom Score questionnaire. Biochemical control was determined using the nadir+2 ng/ml definition.

Results: The mean and median followup was 58 and 54 months respectively (range: 24-110 months). The NCCN risk classification for FR and IR patients were used. 125I sources were used for 93% of the implants, and 103Pd for 7%. 89% of patients presented with FR disease while 10% presented with IR, and in 2 cases HR. (1%). The median number of sources and total activity implanted were 65 and 999MBq, respectively. The median prostate volume implanted was 36 cc. The median V100 was 95%. Absolute BNED was 97%. The 10 year actuarial probability of biochemical control rate for all patients was 95%, with no difference observed between FR or IR patients (97% and 95% respectively) Late Gu and Gi Grade 2 and higher toxicity was very low. With a minimum follow-up for 2 years, the late Grade 2 and Grade 3 GU toxicity was 19% and 1% respectively. The late Grade 2 and 3 rectal bleeding rate was 1% and 0% respectively, with no Grade 4 toxicity observed.

Conclusion: With extended follow-up of 10 years, real-time IO-PSI demonstrated excellent biochemical control rates with low incidence of toxicity confirming the validity of our original hypothesis and methodology of Inverse planning in real time for PSI, and comparing favorably to other alternatives at lower cost in the USA.

PO-0980
Inhibition of STAT3 enhances the radiosensitising effect of Temozolomide in Glioblastoma model
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Purpose or Objective: Despite aggressive treatment with radiation therapy plus temozolomide (TMZ), the prognosis for glioblastoma remains poor. We investigated the potential of targeting signal transducer and activator of transcription-3 (STAT3) to improve the therapeutic outcome of glioblastoma.

Material and Methods: We evaluated the preclinical potential of a STAT3 inhibitor, Cpd188 combined with temozolomide and radiation in vitro assays using two established glioblastoma cell lines (U251, U87) and two patients-derived glioblastoma cell lines (GBL12, GBL28) and in vivo studies using nude mice bearing intracranial U251 xenografts.

Results: Cpd188 potentiated the radiosensitizing effect of TMZ in U251 cell which has high levels of p-STAT3 expression. Increased radiosensitizing effects of TMZ were associated with impaired DNA damage repair, apoptosis and the reversion of epithelial-mesenchymal transition (EMT). Cpd188 delayed in vivo tumor growth both alone and in combination
with radiation and TMZ. We also confirmed the radiosensitizing effect of Cpd188 of GBL28 cell which was originated from a patient with high level of STAT3 expression and unmethylated MGMT.

Conclusion: Targeting STAT3 using Cpd188 could be a viable therapeutic approach to improve the outcome of current standard therapy for glioblastoma patients having high p-STAT3 expression regardless of MGMT methylation status. Work supported by the grant (#2013R1A1A2074531) from the Ministry of Science, ICT & Future Planning to In Ah Kim.

PO-0981
Activation of immune cells and enhanced efficacy of radiotherapy by anti-TIP1 antibodies in cancer

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Purpose or Objective: Purpose: Stress responses in cancer cells are exaggerated over that of normal tissues include signal transduction pathways such as GRP78, PKC, PLC, Rho and others. Many of these regulators of cell viability translocate of the cell membrane during the stress response. Mechanisms of protein transport include motor and scaffold proteins such as Tax Interacting protein-1 (TIP-1), which translocates to the surface of the cell membrane of cancer cells following exposure to ionizing radiation. TIP1 is a scaffold protein that moves proteins to and from the cell membrane. It is over expressed in poor prognosis cancers.

Material and Methods: Methods: We studied radiation induction of TIP1 by western immunoblot and flow cytometry. We used siRNA to knock down TIP1 in human GBM and NSCLC cell lines. We utilized Anti-TIP1 antibodies administered IV to mouse models of human cancer xenograft tumors. Significant levels of the TIP-1 membrane protein were also present in the irradiated tumors, but not in untreated controls, as demonstrated by immunohistochemistry. Near-infrared imaging studies showed significant targeting and binding of anti-TIP-1 Ab to irradiated tumors compared to untreated tumors and IgG controls at 72 hrs. Knockdown of TIP1 and blocking Abs that bind to the PDZ domain of this protein were administered IV to mice bearing irradiated human cancers.

Results: Results: Membrane protein western blots showed a significant increase in the expression of TIP-1 protein at 4 and 24 hrs following irradiation with 3 Gy as compared to 0 Gy untreated control tumors. Significant levels of the TIP-1 membrane protein were also present in the irradiated tumors, but not in untreated controls, as demonstrated by immunohistochemistry. News-infrared imaging studies showed significant targeting and binding of anti-TIP-1 Ab to irradiated tumors compared to untreated tumors and IgG controls at 72 hrs. Knockdown of TIP1 and blocking Abs that bind to the PDZ domain of TIP1 enhance cytotoxicity in cancer but not normal tissues. Anti-PDZ-domain Abs significantly enhanced cytotoxicity in DS4, H1299, H460 and A549 human cancer cells. We studied the mechanisms by which the Abs enhance cytotoxicity and improve tumor control. Abs activate caspases 2, 3/7 in irradiated cancers. Moreover, Anti-TIP1 antibodies bound to the surface of cancer cells activated immune effector cells. In mouse models of human cancers, Anti- TIP1 Abs enhanced tumor growth delay after radiotherapy when administered IV to mouse models of human cancer.

Conclusion: Conclusion: Anti- TIP1 antibodies activate immune effector cells and enhance the efficacy of radiotherapy specifically in cancer without enhancing the responses to normal tissues. TIP1 is a new target for the development of novel radiation sensitizing agents.