

COMMENTARY

Open Access

# Stereotactic iodine-125 brachytherapy for brain tumors: temporary versus permanent implantation

Maximilian I Ruge<sup>1\*</sup>, Philipp Kickingereeder<sup>1</sup>, Stefan Grau<sup>2</sup>, Harald Treuer<sup>1</sup>, Volker Sturm<sup>1</sup> and Juergen Voges<sup>3</sup>

## Abstract

Stereotactic brachytherapy (SBT) has been described in several publications as an effective, minimal invasive and safe highly focal treatment option in selected patients with well circumscribed brain tumors <4 cm. However, a still ongoing discussion about indications and technique is hindering the definition of a clear legitimation of SBT in modern brain tumor treatment. These controversies encompass the question of how intense the irradiation should be delivered into the target volume (dose rate). For instance, reports about the use of high dose rate (HDR) implantation schemes (>40 cGy/h) in combination with adjuvant external beam radiation and/or chemotherapy for the treatment of malignant gliomas and metastases resulted in increased rates of radiation induced adverse tissue changes requiring surgical intervention. Vice versa, such effects have been only minimally observed in numerous studies applying low dose rate (LDR) regimens (3–8 cGy/h) for low grade gliomas, metastases and other rare indications. Besides these observations, there are, however, no data available directly comparing the long term incidences of tissue changes after HDR and LDR and there is, furthermore, no evidence regarding a difference between temporary or permanent LDR implantation schemes. Thus, recommendations for effective and safe implantation schemes have to be investigated and compared in future studies.

**Keywords:** Stereotactic Brachytherapy, Permanent/Temporary Low Dose Rate Implantation, Brain Tumors

Stereotactic implantation of irradiation sources (so called stereotactic brachytherapy (SBT)) has been applied for intrinsic brain tumors and metastases for more than four decades in numerous patients. The majority of studies reported about the application of high-dose rate (HDR) iodine-125 implants (40-70 cGy/h) for high-grade gliomas, including two prospective randomized trials, which compared standard treatment regimens with/without SBT [1,2]. This approach, however, was associated with high incidence of radiation induced adverse effects requiring repeated surgery and failed to proof any significant oncological benefit as compared to standard treatment regimens. Another approach using SBT was the application of low-dose rate (LDR) implants (3-8 cGy/h) for slow growing low-grade gliomas or brain

metastases which demonstrated in several very recent publications to be associated with only little permanent deficits and almost an absence of radiation induced necrosis [3-17].

A recent comprehensive review on SBT for brain tumors by Schwarz et al. [17] summarized almost all published knowledge about this technique with the clear intention to clarify and overcome some of the preconceptions associated with brachytherapy. The authors elucidated in this well written and thoroughly investigated review the rationale, physical and biological characteristics, surgical technique, indications, complications and – most important – evidence in a critical and comprehensive manner. Especially laudable is the authors' clear recommendation to LDR implantation schemes instead of HDR as used by US groups in treatment protocols for high grade gliomas which caused unacceptable high rates of treatment relevant radiation induced necrosis [1,18,19].

Since over two decades our group also applies stereotactic iodine-125 brachytherapy in now over

\* Correspondence: maximilian.ruge@uk-koeln.de

<sup>1</sup>Department for Stereotaxy and Functional Neurosurgery, University of Cologne, Kerpener Straße 62, Cologne 50937, Germany

Full list of author information is available at the end of the article

1200 patients for the treatment of - predominantly low-grade - brain tumors. Based on this experience we would like to contribute the following aspects to the discussion:

1. Schwarz et al. mention an increased risk for prolonged edema and late radiation necrosis when using permanent implantation as compared to temporary LDR implantation and refer to non human experimental data of the mid 1980's [20-22]. Our applied prospective treatment protocol for low grade gliomas (WHO grades I and II) stipulates permanent implantation of iodine-125 seeds with initial dose rates of 0.02 – 0.03 Gy/h (prescribed surface dose: 50–65 Gy). With this strategy we very rarely observe prolonged edema or late radiation necrosis [3,4,6,7]. Interestingly, the rate of surgically relevant cysts after temporary implantation of iodine-125 seeds for low grade gliomas in a pediatric population as reported by Korinthenberg et al. [10] was three times as high (33/94 patients = 35.1 %) as in a similar population treated with permanent implants by our group (16/142 Patients = 11.3 %) [3].

Furthermore, Kreth et al. evaluated risk factors for SBT in 515 patients with low grade brain tumors and mentioned no significant difference of temporary vs. permanent LDR implantation schemes with regard to complications [23]. Thus, our clinical experience as well as the reported findings in the literature does not support at all the authors' reservation towards permanent implantation SBT.

However, a critical comparison of long term results with regard to radiation induced tissue changes between permanent vs. temporary LDR implantation schemes is yet not available but necessary to ultimately clarify this controversy [24].

2. To complement the review's physics part we may indicate that the Task Group 43 of the AAPM (American Academy of Physical Medicine) introduced (beginning in 1995) an internationally accepted standard for the dosimetry of iodine-125 seeds allowing to compare dosimetry between different countries and groups [25-30].

3. Further, we concur with Schwarz et al. on the importance of post operative imaging (either by intraoperative X-ray or by postoperative CT scanning) to confirm an accurate location of the implanted seeds, thus allowing a precise comparison with the irradiation plan at any time [31].

Ultimately, publications of this high quality keep one of oldest and most sophisticated neurosurgical technique in a vivid discussion as a minimal invasive, safe, and highly effective neuro-oncological local treatment option for selected patient populations.

## Abbreviations

SBT: Stereotactic Brachytherapy; HDR: High Dose Rate; LDR: Low Dose Rate; cGy/h: Centigray Per Hour; AAPM: American Academy of Physical Medicine.

## Author details

<sup>1</sup>Department for Stereotaxy and Functional Neurosurgery, University of Cologne, Kerpener Straße 62, Cologne 50937, Germany. <sup>2</sup>Department for Neurosurgery, University of Cologne, Kerpener Straße 62, Cologne 50937, Germany. <sup>3</sup>Department of Stereotactic Neurosurgery, University of Magdeburg, Leipziger Str. 44, Magdeburg 39120, Germany.

Received: 16 May 2012 Accepted: 19 June 2012

Published: 19 June 2012

## References

1. Laperriere NJ, Leung PM, McKenzie S, Milosevic M, Wong S, Glen J, Pintilie M, Bernstein M: **Randomized study of brachytherapy in the initial management of patients with malignant astrocytoma.** *Int J Radiat Oncol Biol Phys* 1998, **41**(5):1005–1011.
2. Selker RG, Shapiro WR, Burger P, Blackwood MS, Arena VC, Gilder JC, Malkin MG, Mealey JJ Jr, Neal JH, Olson J, Robertson JT, Barnett GH, Bloomfield S, Albright R, Hochberg FH, Hiesiger E, Green S: **The Brain Tumor Cooperative Group NIH Trial 87-01: a randomized comparison of surgery, external radiotherapy, and carmustine versus surgery, interstitial radiotherapy boost, external radiation therapy and carmustine.** *Neurosurgery* 2002, **51**(2):343–355. discussion 355–347.
3. Ruge MI, Simon T, Suchorska B, Lehrke R, Hamisch C, Koerber F, Maarouf M, Treuer H, Berthold F, Sturm V, Voges J: **Stereotactic brachytherapy with iodine-125 seeds for the treatment of inoperable low-grade gliomas in children: long-term outcome.** *J Clin Oncol* 2011, **29**(31):4151–4159.
4. Suchorska B, Ruge M, Treuer H, Sturm V, Voges J: **Stereotactic brachytherapy of low-grade cerebral glioma after tumor resection.** *Neuro Oncol* 2011, **13**(10):1133–1142.
5. Kreth F, Faist M, Grau S, Ostertag C: **Interstitial 125I radiosurgery of supratentorial de novo WHO Grade 2 astrocytoma and oligoastrocytoma in adults: long-term results and prognostic factors.** *Cancer* 2006, **106**(6):1372–1381.
6. Voges J, Treuer H, Schlegel W, Pastyr O, Sturm V: **Interstitial irradiation of cerebral gliomas with stereotactically implanted iodine-125 seeds.** *Acta Neurochir Suppl (Wien)* 1993, **58**:108–111.
7. Voges J, Sturm V: **Interstitial irradiation with stereotactically implanted I-125 seeds for the treatment of cerebral glioma.** *Crit Rev Neurosurg* 1999, **9**(4):223–233.
8. Peraud A, Goetz C, Siefert A, Tonn JC, Kreth FW: **Interstitial iodine-125 radiosurgery alone or in combination with microsurgery for pediatric patients with eloquently located low-grade glioma: a pilot study.** *Childs Nerv Syst* 2007, **23**(1):39–46.
9. Schnell O, Scholler K, Ruge M, Siefert A, Tonn JC, Kreth FW: **Surgical resection plus stereotactic 125I brachytherapy in adult patients with eloquently located supratentorial WHO grade II glioma - feasibility and outcome of a combined local treatment concept.** *J Neurol* 2008, **255**(10):1495–1502.
10. Korinthenberg R, Neuburger D, Trippel M, Ostertag C, Nikkhah G: **Long-term results of brachytherapy with temporary iodine-125 seeds in children with low-grade gliomas.** *Int J Radiat Oncol Biol Phys* 2011, **79**(4):1131–1138.
11. Kreth FW, Warnke PC, Ostertag CB: **Interstitial radiosurgery of low grade glioma.** *Nervenarzt* 1993, **64**(10):633–639.
12. Ostertag CB, Kreth FW: **Iodine-125 interstitial irradiation for cerebral gliomas.** *Acta Neurochir (Wien)* 1992, **119**(1–4):53–61.
13. Ostertag CB: **Stereotactic interstitial radiotherapy for brain tumors.** *J Neurosurg Sci* 1989, **33**(1):83–89.
14. Ruge MI, Suchorska B, Maarouf M, Runge M, Treuer H, Voges J, Sturm V: **Stereotactic 125Iodine Brachytherapy for the Treatment of Singular Brain Metastases: Closing a Gap?** *Neurosurgery* 2011, **68**(5):1209–1219.
15. Ruge MI, Kickingeder P, Grau S, Hoevens M, Treuer H, Sturm V: **Stereotactic biopsy combined with stereotactic (125I)iodine brachytherapy for diagnosis and treatment of locally recurrent single brain metastases.** *J Neurooncol* 2011, **105**(1):109–118.
16. Ruge MI, Kocher M, Maarouf M, Hamisch C, Treuer H, Voges J, Sturm V: **Comparison of stereotactic brachytherapy (125 iodine seeds) with**

- stereotactic radiosurgery (LINAC) for the treatment of singular cerebral metastases. *Strahlenther Onkol* 2011, **187**(1):7–14.
17. Schwarz SB, Thon N, Nikolajek K, Niyazi M, Tonn JC, Belka C, Kreth FW: **Iodine-125 brachytherapy for brain tumours - a review.** *Radiat Oncol* 2012, **7**(1):30.
  18. Gutin PH, Prados MD, Phillips TL, Wara WM, Larson DA, Leibel SA, Sneed PK, Levin VA, Weaver KA, Silver P, et al: **External irradiation followed by an interstitial high activity iodine-125 implant "boost" in the initial treatment of malignant gliomas: NCOG study 6 G-82-2.** *Int J Radiat Oncol Biol Phys* 1991, **21**(3):601–606.
  19. Scharfen CO, Sneed PK, Wara WM, Larson DA, Phillips TL, Prados MD, Weaver KA, Malec M, Acord P, Lamborn KR, et al: **High activity iodine-125 interstitial implant for gliomas.** *Int J Radiat Oncol Biol Phys* 1992, **24**(4):583–591.
  20. Groothuis DR, Wright DC, Ostertag CB: **The effect of 125I interstitial radiotherapy on blood-brain barrier function in normal canine brain.** *J Neurosurg* 1987, **67**(6):895–902.
  21. Fike JR, Cann CE, Phillips TL, Bernstein M, Gutin PH, Turowski K, Weaver KA, Davis RL, Higgins RJ, DaSilva V: **Radiation brain damage induced by interstitial 125I sources: a canine model evaluated by quantitative computed tomography.** *Neurosurgery* 1985, **16**(4):530–537.
  22. Ostertag CB: **Brachytherapy-interstitial implant radiosurgery.** *Acta Neurochir Suppl (Wien)* 1993, **58**:79–84.
  23. Kreth FW, Faist M, Rossner R, Birg W, Volk B, Ostertag CB: **The risk of interstitial radiotherapy of low-grade gliomas.** *Radiother Oncol* 1997, **43**(3):253–260.
  24. Liu BL, Cheng JX, Zhang X, Zhang W: **Controversies concerning the application of brachytherapy in central nervous system tumors.** *J Cancer Res Clin Oncol* 2010, **136**(2):173–185.
  25. Nath R, Anderson LL, Luxton G, Weaver KA, Williamson JF, Meigooni AS: **Dosimetry of interstitial brachytherapy sources: recommendations of the AAPM Radiation Therapy Committee Task Group No. 43.** *American Association of Physicists in Medicine.* *Med Phys* 1995, **22**(2):209–234.
  26. Williamson JF, Coursey BM, DeWerd LA, Hanson WF, Nath R, Ibbott G: **Guidance to users of Nycomed Amersham and North American Scientific, Inc., I-125 interstitial sources: dosimetry and calibration changes: recommendations of the American Association of Physicists in Medicine Radiation Therapy Committee Ad Hoc Subcommittee on Low-Energy Seed Dosimetry.** *Med Phys* 1999, **26**(4):570–573.
  27. Williamson JF, Coursey BM, DeWerd LA, Hanson WF, Nath R, Rivard MJ, Ibbott G: **On the use of apparent activity (Aapp) for treatment planning of 125I and 103Pd interstitial brachytherapy sources: recommendations of the American Association of Physicists in Medicine radiation therapy committee subcommittee on low-energy brachytherapy source dosimetry.** *Med Phys* 1999, **26**(12):2529–2530.
  28. Williamson JF, Butler W, Dewerd LA, Huq MS, Ibbott GS, Mitch MG, Nath R, Rivard MJ, Todor D: **Recommendations of the American Association of Physicists in Medicine regarding the impact of implementing the 2004 task group 43 report on dose specification for 103Pd and 125I interstitial brachytherapy.** *Med Phys* 2005, **32**(5):1424–1439.
  29. Kubo HD, Coursey BM, Hanson WF, Kline RW, Seltzer SM, Shuping RE, Williamson JF: **Report of the ad hoc committee of the AAPM radiation therapy committee on 125I sealed source dosimetry.** *Int J Radiat Oncol Biol Phys* 1998, **40**(3):697–702.
  30. Rivard MJ, Coursey BM, DeWerd LA, Hanson WF, Huq MS, Ibbott GS, Mitch MG, Nath R, Williamson JF: **Update of AAPM Task Group No. 43 Report: A revised AAPM protocol for brachytherapy dose calculations.** *Med Phys* 2004, **31**(3):633–674.
  31. Treuer H, Klein D, Maarouf M, Lehrke R, Voges J, Sturm V: **Accuracy and conformity of stereotactically guided interstitial brain tumour therapy using I-125 seeds.** *Radiother Oncol* 2005, **77**(2):202–209.

doi:10.1186/1748-717X-7-94

**Cite this article as:** Ruge et al.: Stereotactic iodine-125 brachytherapy for brain tumors: temporary versus permanent implantation. *Radiation Oncology* 2012 **7**:94.

**Submit your next manuscript to BioMed Central and take full advantage of:**

- **Convenient online submission**
- **Thorough peer review**
- **No space constraints or color figure charges**
- **Immediate publication on acceptance**
- **Inclusion in PubMed, CAS, Scopus and Google Scholar**
- **Research which is freely available for redistribution**

Submit your manuscript at  
www.biomedcentral.com/submit

