# Adjuvant Radiotherapy Following Surgical Resection of Pituitary Adenomas: a Systematic Review and Meta-Analysis of 7679 Patients

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## Introduction

Post-operative radiotherapy has been shown to improve tumor control and recurrence-free survival in patients with pituitary adenomas. However, due to the potential for complications and long-term side effects, the role of adjuvant radiotherapy in this setting remains unclear. This study aims to address this gap in the clinical management of patients with pituitary adenomas, and to determine the efficacy and safety of post-operative radiotherapy.

## Methods

PubMed, MEDLINE and Cochrane databases were searched, with no language or publication date restrictions. Studies were included if they reported on patients treated post-operatively with any form of radiation therapy. Studies reporting on both functioning and non-functioning pituitary adenomas were included. Forest plots were generated to determine a pooled event rate and 95% confidence interval (CI) for each outcome using a random effect model analysis.

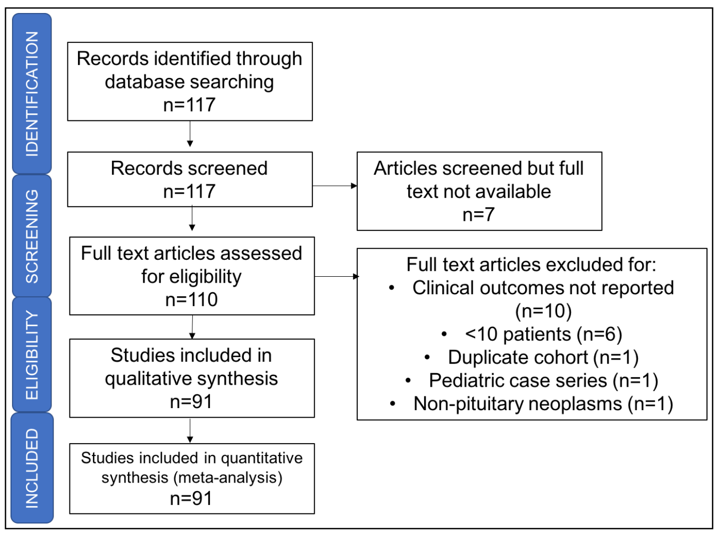
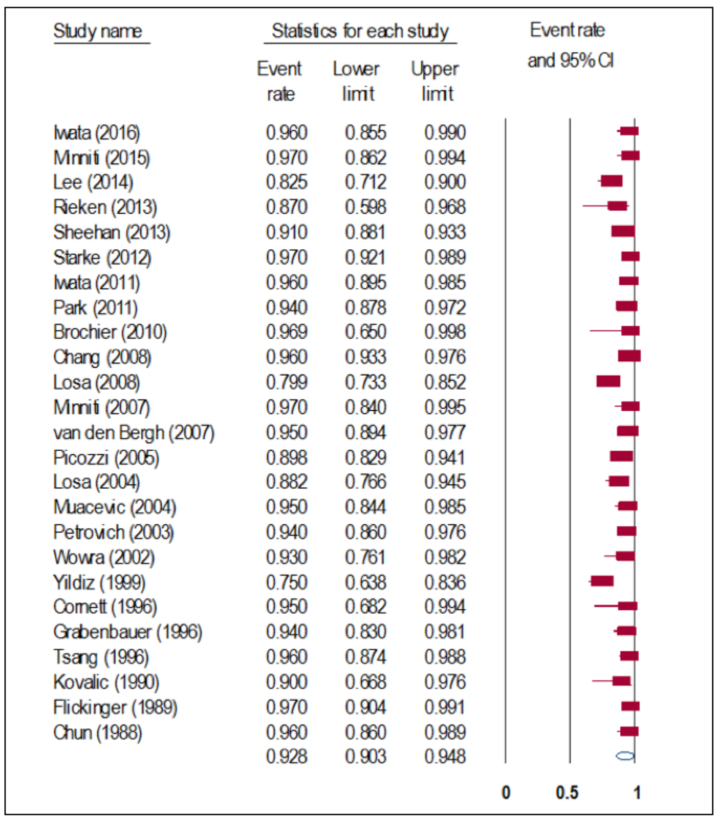



**Figure 1. Search strategy.**

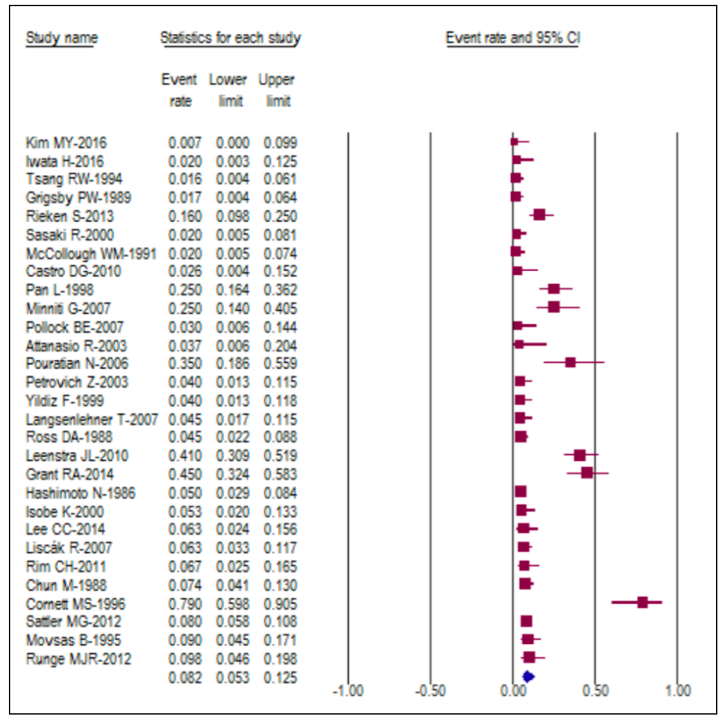
## Results

A total of 89 studies from 1986-2017 met the inclusion criteria, consisting of 7679 cumulative patients. Studies included patients with functioning adenomas only (n=24), non-functioning adenomas only (n=31) or both (n=36). The median age of all patients was 50 years, with a median follow-up duration of 60 months across all studies. The cumulative 5- and 10-year progression-free survival rates were 90.8% (95% CI 86-94%) and 88.6% (95% CI 81-93%), respectively. The overall adverse events rate was 8% (95% CI 5-12%). All outcomes were associated with significant heterogeneity (I2 = 70%). There were no differences in survival rates or adverse events in relation to study date, tumor pathology, radiosurgery system used or dose of radiation.

**Figure 2. 5-year progression-free survival across studies.**




| Study name | Event rate | Lower limit | Upper limit |
|---|---|---|---|
| Iwata (2016) | 0.960 | 0.855 | 0.990 |
| Minniti (2015) | 0.970 | 0.862 | 0.994 |
| Lee (2014) | 0.825 | 0.712 | 0.900 |
| Rieken (2013) | 0.870 | 0.598 | 0.968 |
| Sheehan (2013) | 0.910 | 0.881 | 0.933 |
| Starke (2012) | 0.970 | 0.921 | 0.989 |
| Iwata (2011) | 0.960 | 0.895 | 0.985 |
| Park (2011) | 0.940 | 0.878 | 0.972 |
| Brochier (2010) | 0.969 | 0.650 | 0.998 |
| Chang (2008) | 0.960 | 0.933 | 0.976 |
| Losa (2008) | 0.799 | 0.733 | 0.852 |
| Minniti (2007) | 0.970 | 0.840 | 0.995 |
| van den Bergh (2007) | 0.950 | 0.894 | 0.977 |
| Picozzi (2005) | 0.898 | 0.829 | 0.941 |
| Losa (2004) | 0.882 | 0.766 | 0.945 |
| Muacevic (2004) | 0.950 | 0.844 | 0.985 |
| Petrovich (2003) | 0.940 | 0.860 | 0.976 |
| Wowra (2002) | 0.930 | 0.761 | 0.982 |
| Yildiz (1999) | 0.750 | 0.638 | 0.836 |
| Cornett (1996) | 0.950 | 0.682 | 0.994 |
| Grabenbauer (1996) | 0.940 | 0.830 | 0.981 |
| Tsang (1996) | 0.960 | 0.874 | 0.988 |
| Kovalic (1990) | 0.900 | 0.668 | 0.976 |
| Flickinger (1989) | 0.970 | 0.904 | 0.991 |
| Chun (1988) | 0.960 | 0.860 | 0.989 |
| | 0.928 | 0.903 | 0.948 |




| Study name | Event rate | Lower limit | Upper limit |
|---|---|---|---|
| Kim MY-2016 | 0.007 | 0.000 | 0.099 |
| Iwata H-2016 | 0.020 | 0.003 | 0.125 |
| Tsang RW-1994 | 0.016 | 0.004 | 0.061 |
| Grigsby PW-1989 | 0.017 | 0.004 | 0.064 |
| Rieken S-2013 | 0.160 | 0.098 | 0.250 |
| Sasaki R-2000 | 0.020 | 0.005 | 0.081 |
| McCollough WM-1991 | 0.020 | 0.005 | 0.074 |
| Castro DG-2010 | 0.026 | 0.004 | 0.152 |
| Pan L-1998 | 0.250 | 0.164 | 0.362 |
| Minniti G-2007 | 0.250 | 0.140 | 0.405 |
| Pollock BE-2007 | 0.030 | 0.006 | 0.144 |
| Attanasio R-2003 | 0.037 | 0.006 | 0.204 |
| Pouratian N-2006 | 0.350 | 0.186 | 0.559 |
| Petrovich Z-2003 | 0.040 | 0.013 | 0.115 |
| Yildiz F-1999 | 0.040 | 0.013 | 0.118 |
| Langsenlehner T-2007 | 0.045 | 0.017 | 0.115 |
| Ross DA-1988 | 0.045 | 0.022 | 0.088 |
| Leenstra JL-2010 | 0.410 | 0.309 | 0.519 |
| Grant RA-2014 | 0.450 | 0.324 | 0.583 |
| Hashimoto N-1986 | 0.050 | 0.029 | 0.084 |
| Isobe K-2000 | 0.053 | 0.020 | 0.133 |
| Lee CC-2014 | 0.063 | 0.024 | 0.156 |
| Liscák R-2007 | 0.063 | 0.033 | 0.117 |
| Rim CH-2011 | 0.067 | 0.025 | 0.165 |
| Chun M-1988 | 0.074 | 0.041 | 0.130 |
| Cornett MS-1996 | 0.790 | 0.598 | 0.905 |
| Sattler MG-2012 | 0.080 | 0.058 | 0.108 |
| Movsas B-1995 | 0.090 | 0.045 | 0.171 |
| Runge MJR-2012 | 0.098 | 0.046 | 0.198 |
| | 0.082 | 0.053 | 0.125 |

**Figure 3. Incidence of complications across studies.**

## Conclusions

This study is one of the largest and most comprehensive surveys of the literature pertaining to adjuvant radiotherapy for pituitary adenomas. Our findings demonstrate that post-operative radiotherapy for pituitary adenomas is effective and safe. Further prospective studies are needed to delineate specific rates of adverse outcomes, as well as the optimal timing of administration of post-operative radiotherapy.